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A Record of the Progress of Pharmacy and the Allied Sciences

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THE AMERICAN
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VOL. 104 APRIL, 1932 NO. 4

EDITORIAL

THE PHILADELPHIA INSTITUTE FOR MEDICAL RESEARCH

THE Philadelphia Institute for Medical Research has been established for "fostering medical research, either by its own initiative or by affiliation and collaboration with medical and allied institutions desiring to establish such relationship," and will begin its work in the autumn under the directorship of Dr. Leonard G. Rowntree, now director of clinical investigation, Mayo Clinic, Rochester, Minnesota, and professor of medicine, University of Minnesota. Its president is Dr. Judson Daland, professor of medicine, Medical Department, University of Pennsylvania.

Dr. Leonard G. Rowntree

President Daland states that:

"Research in medicine in the past has come largely through contributions from universities, medical schools, and their hospitals and clinics. More recently, because of urgent need, special institutions of research have been created in certain of the great cities in Europe and this country, the best known being the Pasteur Institute in Paris, the Rockefeller Institute for Medical Research in New York City, and one of quite recent date, the Thorndike Laboratory in the Boston City Hospital. All of these institutes have made tremendous and permanent contributions to medicine, and added much to the welfare of mankind.

"The Philadelphia Institute for Medical Research will concern itself with what is termed clinical investigation—that is, the study

of the sick and the diseases from which they suffer; including, also, pharmacological research.

"Research will be made for methods of value for the prevention of disease, and for improvements in methods of diagnosis and treatment, especially in the earlier stages. Studies will be carried on, also, in the fundamental branches of science underlying medical knowledge."

The new Institute will center its activities in the Philadelphia General Hospital. A site on the hospital grounds has been assigned for the erection of a building when funds are available, but, temporarily, the Institute will occupy quarters in a new building under construction, and will function in association with the hospital staffs.

The creation of the Institute resulted from a centenary celebration in 1922 of the birth of Pasteur by a group of Philadelphia physicians. The charter members were: the late Dr. William Duffield Robinson; Admiral William C. Braisted, Surgeon General of the U. S. Navy retired, and former president of the Philadelphia College of Pharmacy and Science; Dr. Judson Daland; the late Dr. Francis X. Dercum; Dr. McCluney Radcliffe; the late Edgar Fahs Smith, who was provost of the University of Pennsylvania; Dr. Charles A. E. Codman; the late Hampton L. Carson, who was Attorney General of Pennsylvania, and Mr. Joseph Carson.

The new director, Dr. Rowntree was chosen by reason of his "outstanding knowledge, enthusiasm, training and proven ability to lead in all questions concerning medical research." He was born in London, Ontario, in 1884. He was graduated in medicine from the University of Western Ontario in 1905, and served an interneship at the Victoria Hospital. Then he practiced medicine for two years in Camden, N. J., while engaged in research studies and duties at the Jefferson Medical College, the Medical Department of the University of Pennsylvania and the Philadelphia General Hospital. In 1907 he served in the Medical Department of the Johns Hopkins Hospital, and as voluntary assistant in pharmacology, and associate professor of medicine. In 1916 he was made professor of medicine of the University of Minnesota, and later became chief of the Department of Medicine.

During the World War, he saw service in France with the Air Service Medical Staff. He was naturalized during the war period. He is a colonel in the Medical Reserve of the American Army.

In 1920 he went to the Mayo Clinic as head of the Medical Section. Two years later he was made chief of the medical division of the Mayo Foundation. Later he was advanced to the post of senior medical consultant and the directorship of Clinical Investigation of the Mayo Clinic.

The membership of the various boards of the Institute is as follows:

Trustees—Governor of the State of Pennsylvania, ex-officio; Mayor of Philadelphia, ex-officio; Commissioner of Health of Pennsylvania, ex-officio; Director of Public Health of Philadelphia, ex-officio; Dr. Judson Daland, president; Dr. Charles A. E. Codman, vice-president; C. Wilson Roberts, secretary; William Fulton Kurtz, treasurer; Joseph Carson, counsellor; Dr. John D. McLean and Dr. McCluney Radcliffe.

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The establishment of the Philadelphia Institute for Medical Research is a most important forward step for promoting the growth and development, not only of medical science, but indirectly, of pharmaceutical and allied sciences, and is deserving of the heartiest support.

J. W. ENGLAND.

COMMENCEMENT

MUSIC, flowers, presents, pretty girls, jewels, laces, furbelows. Processions, mortar boards, academic gowns, reunions, dinners, dances, games, oratory, prizes. sheepkins, and "rah, rah."

It's a glorious time. But commencement is only the beginning.

Where will the newly fledged graduate go when the red fire burns out and he starts on the real voyage of life?

He may buy a store, become a manager, a prescription clerk, a soda water server, a traveling salesman, start a pine board cut-rate shop, take up research, become a manufacturer, exploit a patent medicine, enter politics, or become a real estate broker.

The seas upon which the young graduate may set sail are boundless.

The roads upon which he may travel may lead to success or to disaster. They are not paved with gold.

Diplomas are not passports to the promised land. The ladder must be mounted round by round.

If the new graduate is wise he will always be a pharmacist. He will cling to his Alma Mater, join in association work, read the journals, and keep abreast of the progress of science and the trend of trade. He will do well to take on active citizenship and join his fellow men in promoting the welfare of his community.

Science changes. Medicine and pharmacy change, sometimes swiftly. The new graduate must be prepared to meet the change. Whatever his patrons need for their health, their well-being, and their happiness it will be his province to supply. He must continuously give a higher, a better, and an ever-growing service. He must fill the needs of the age in which he may live and of the humanity which he may serve.

Among the throngs at commencement time there comes the old graduate. He has stooping shoulders. He is gray, bald, wrinkled. His joints are stiffened and his eyes are dimmed. He finds that for the most part his classmates are dead. Pharmacy has gone to the "bow-wows." He longs for the "good old days." He walks in the fog of gloom and despair.

What is there in commencement for the graduate of other days? If he looks at it rightly, commencement offers a great opportunity. The college is his college. He should renew his vows to Alma Mater.

His college needs his moral, spiritual and material support. Every step forward adds a star to his diploma. The doors of his college stand wide open to him. Library, museum, equipment, faculty, are at his service. Some of our colleges have installed model stores wherein are displayed the most modern types of store arrangement, equipment, methods of display and merchandising. The veteran should go back to school. While life lasts he should be a student. Some of our colleges are establishing courses especially adapted to "back-number" graduates.

The veteran pharmacist should never reach the stage of the "sere and faded leaf." For him there should be no years of decline. It has been found possible to keep people at the peak of their powers while their years increase. Let the veteran be of good cheer. Thirty or forty years from now there will be twice as many old people as we have today.

In the days "just around the corner" cool, analytical brain power will be needed. The burden of the younger men will be lighter and steps saved if they can avail themselves of the wisdom of their elders.

For the veteran and for the new graduate commencement may well be made a time for rejoicing, a time for "rah, rah." It should also become for each a time of real beginning.

FRED B. KILMER.

ORIGINAL ARTICLES

OUR EDUCATIONAL HERITAGE*

By Professor C. Leonard O'Connell

Pittsburgh College of Pharmacy, Pittsburgh, Penna.

TODAY we are assembled to celebrate in a formal way the anniversary of the founding of the Philadelphia College of Pharmacy and Science, the oldest college of pharmacy in the new world. For the most part, those gathered here are alumni of this institution or have some close bond that makes this occasion one of particular significance to them. In a broader way, all those interested in pharmacy may give pause today in their busy workaday lives to consider deeply the thoughts and aspirations that motivated the men who launched this institution more than a century ago. The speaker has selected for his subject the following: "Our Educational Heritage." The intention shall be to set forth briefly the unfolding of the educational ideal from the beginning to the present day. Then a suggestive future trend will be developed in the light of the educational experience of outstanding educators in various fields. The title serves to emphasize that, while this old institution is the particular heritage of the sons and daughters of the Philadelphia College of Pharmacy and Science, it is also the general heritage of the sons and daughters of all American pharmacy.

Education in pharmacy antedates colleges of pharmacy. Before we had colleges of pharmacy men and women were trained for their vocation in the pharmacy itself. In this plan the training given to the neophytes was directly supervised by the master, an apothecary who generally took his responsibility seriously and attempted to acquaint the apprentice with the material that experience indicated would be necessary in order that the prospective pharmacist might be in position to function effectively in his field. Such a training was by its very nature essentially pragmatic, since it had as its dominant note the practical problems or fact data with which the pharmacist would have to deal. This note coupled with the fact that the field of knowledge canvassed in a study of pharmacy was quite extensive

*Founder's Day Address, February 22, 1932.

resulted in making the training process one of question and answer and militated greatly against any possibility of developing adequate reasoning ability, which ability is generally conceded to be the mark of a truly educated person. While there were many unusual products of this system most people would perforce agree that these good products resulted despite the system rather than because of it. Most men educated under this system were technicians essentially, quite often very proficient in the manual operations required in their work, but less frequently were they thoroughly conversant with the principles upon which the art is based.

As the importance of the pharmacist's supreme function of supplementing the work of the physician by compounding and dispensing drugs and medicines captured the attention of those vitally interested in advancing their vocation, it became clearly apparent that a great need existed for an agency that would educate students in a more formal way. Out of this urge came the establishment of the first college whose anniversary we are celebrating today. This departure in method is a truly significant contribution, for it marked the beginning of a plan to set men apart whose chief duty it would be to devote themselves to a careful consideration of the educational needs of those who came to them for guidance and equipment for life.

In the early colleges of pharmacy it was natural to expect that the educational procedure would be greatly influenced by the old preceptorial methods which, indeed, was the case. For the most part the early schools of pharmacy were sort of an elaboration of the old tutorial method and while they marked a distinct advance in the training afforded, yet they were in the main conditioned by what they believed was expected of them in the way of student product, and they seemingly made no earnest attempt to study the problem objectively.

Honesty and candor compel the admission that, in spite of many shortcomings from the pedagogical point of view, many of these early schools did an unusually good job of what they set out to do, namely, produce graduates that were able to do what was expected of them and be safe public servants.

When schools of pharmacy directly connected with universities essayed the task of establishing courses they were at once struck with the fact that the procedure differed in such a marked manner that it was difficult for their department to receive proper recognition from

other departments. The restricted courses in pharmacy coupled with the absence of common cultural material, a necessary and accepted part of most other courses, resulted in a lack of appreciation of the real value of the work of the pharmacist and increased the difficulties of the adequate teaching of the subject matter.

This condition was bound to continue just as long as a degree was given in pharmacy for less than what was ordinarily regarded as the accepted undergraduate period, namely four full years of training. Now that pharmacy has reached the point where, shortly most of the accredited schools will go to a four-year basis, the speaker will propose a formula for a common ground among educators for the establishment of courses that carry with them everything necessary to satisfy real baccalaureate standing, and, in addition, develop in more students a real love of learning so that they will be influenced to carry their study past student days.

In order to determine standards for such education the plan will be to consider material not alone from the fact data side but also from the viewpoint of affording a well-rounded background.

Briefly, one may somewhat polemically state that the problem of pharmaceutical education does not differ essentially from the problem of the College of Liberal Arts except that, in a training in pharmacy, much of the material must be prescribed by the very nature of the field. With more time available in which to educate students formally, *i. e.*, a four-year course instead of a three-year course, but a short time ago a two-year course, there seems to be ample time, if properly availed, to produce men who will be not merely trained technicians but men with a real foundation of a more comprehensive field of human knowledge. Granting, as most fair-minded observers in the field readily will, that pharmacists, on account of their unique social responsibility and important place in the conservation of public health, represent a group whose value would be greatly enhanced by a more thorough training in what is commonly designated as a general education, this opportunity now afforded pharmaceutical educators in planning new courses assumes striking significance. If the increase in time devoted to the education of students in pharmacy is utilized entirely, or for the most part, in elaboration of work now given, great potentiality for gain in prestige will be sacrificed and little improvement will be noted in the products. Feeling that a consideration of the real aim of a college may aid in the solution of the

problem there will follow a brief résumé of expert opinion in the field, which opinions, while necessarily subjective somewhat, yet are quite in line with the available objective data.

Ernest Hatch Wilkins, of the University of Chicago, sets forth his view of the central purpose of the college as follows: "The central purpose of the college is the training of the minds of its students. This training is two fold: it involves, first, the acquisition of knowledge by the student, and, second, training in the processes of the acquisition and the use of knowledge."

The late President Ernest D. Burton said: "A college ought to enable all its students to place themselves in the world, to recognize where they are. It ought to help each student to acquire such a knowledge of the physical universe, of the history of the race, of the structure of society, and of the nature of the individual, that, taking his stand at the center of his own being, he may have a sense of where he is."

While both Professor Wilkins and President Burton are speaking of the college, that is, of liberal arts, yet if one considers the pharmacist as a real focus of influence in his community, which, indeed, he should be, certainly his education should measure up to some such standard as set forth in the foregoing quotations. Undoubtedly much of the inappreciation of the real value of the pharmacist to physicians and to the public may be directly traced to the pharmacist's inability to orient himself in his life's problem.

Viewed in terms of such a standard as suggested above the problem resolves itself into one of producing not merely trained technicians, however safe they may be, but rather men so trained and grounded in the foundations of general knowledge in addition to the necessary fact data in the field, that pharmacy may speedily take its rightful place among the other professions. Briefly pharmacy must be improved from within, and since all competent thinkers are agreed that the prestige of a calling may be safely measured in terms of individuals professing the calling, broader knowledge of the entire field of human endeavor on the part of the pharmacist is imperative.

Further, the intensive training formerly required and to a marked degree still continued, prevents proper development among students of pharmacy of the ability to apply the knowledge they have acquired. Such a condition which all educators know prevails to a high degree really vitiates the end of education, at least, from the

functional viewpoint. In other words, if a student has within him the knowledge to solve a difficulty, but lacks the ability to apply it to specific problems, the information is valueless from the practical viewpoint. To make this condition less prevalent should be part of the business of the college of pharmacy.

President Lowell, of Harvard, states that the aim of college is as follows: "So it is true that the cultivation of the mind by colleges is an attempt to make men think accurately, to discern between the essential and accidental in phenomena, and to train the imagination to grasp things that can not be felt or perceived by the material senses. That is the object of college education. It is not merely to give knowledge. Knowledge vanishes away, but wisdom, I take it, is after all perception of the relative value of things. The real thing we want is not knowledge but resourcefulness. What I mean is that the art which creates things, both great and small, is not the capacity for solving problems. That may seem a curious statement, but the real art of life consists in finding out what is the question to be solved, and the person who can find out what the problem is to be solved is the man who really makes the contributions to life."

Measured in terms of such a criterion, must we not say that our procedure in pharmacy leaves much to be desired, and, if we do not admit this, how may we account for the dearth of resourceful products in our field? While we have been eminently successful in passing on to each succeeding group the knowledge necessary for complete service to the public, yet we have certainly not developed the ability to apply that knowledge to a sufficient degree. Perhaps the fault lies chiefly in the fact that detailed knowledge has been overemphasized, while the ability to apply has either been insufficiently developed or taken for granted.

In recent interviews, two eminent educators have sounded a warning in relation to the danger of the present trend in education with its emphasis upon specialization. Since both of these men speak out of an experience covering half a century certain peculiar authority may be imputed to their utterances, particularly, in view of the fact that similar statements are becoming more frequent and may be ably supported.

Dr. Butler, of Columbia, said recently: "Leisurely reading for pleasure has greatly declined. Young men often feel, if they do read, that it must be for profit, not realizing that they may profit

most from something not directly connected with their particular line of endeavor. Specialization is bound to lead to narrowness. What we need today is not narrow men, but broad men sharpened to a point. In other words, education should begin with breadth and let its applications deal with narrowness, if need be."

Dr. Hibben, of Princeton, spoke as follows: "More and more it has become evident that these days are days of specialization, but this very specialization brings with it a danger that the student may become narrow in his learning. Naturally this must be guarded against, for no college desires to turn out men lacking in general culture. Today education has to a certain degree become a problem of stressing some subjects without neglecting others."

In regard to the essential objective of a college education, Dr. Hibben spoke as follows: "I think I can say that the essential objective of a college education today is the development in the individual student of his potential capacity, evidenced by a growing intellectual vigor and integrity of character. I do not think that this potential element can ever be developed to the full in four years of a college course, but all institutions recognize that there should be a progress in this development."

Certainly most educators in whatever field and certainly those in pharmacy must be struck with the clear statement of danger in specialization as well as the pressing need for inculcating the definite notion that the educative process must be a progressive one, if we desire to produce graduates who will measure up to the proper notion of a college man.

With the inherent danger of narrowness on account of the restricted character of much of the field of pharmacy, educators in planning four-year courses might with advantage approach the problem eye to eye with the college of liberal arts. With such a notion in view there will follow a brief summation in the form of a Tabular Survey of the Field of General Education by Wilkins which indicates the subjects taught in typical colleges. Granting the value of these subjects, at least from the cultural and fact applying sides, we shall then consider a pharmaceutical curriculum that could and the speaker feels should be given in a four-year course. In this consideration of subject matter we shall assume the inclusion of the specific subjects now demanded by the syllabus and observe particularly the ease with which the pharmacy course could be made to approach the liberal arts course both in content and intent.

TABULAR SURVEY OF THE FIELD OF GENERAL EDUCATION.

Physical Sciences	Physical-Social Sciences	Social Sciences	Studies Closely Related to the Social Sciences	Arts	General Mental Tools
	Geography	Sociology	History	Literature	Mathematics
Physics				English and American	
Chemistry	Hygiene	Economics	Philosophy		Logic
			Metaphysics	Foreign	
Astronomy	Psychology	Political Science			English
Geology			Religion	Music	
Botany					Foreign Language
Zoology				Architecture	
Anatomy				Sculpture	
Physiology				Painting	

SUBJECTS SUGGESTED FOR A FOUR YEAR COURSE IN PHARMACY.

Physics	Hygiene	Sociology	History	Literature	Mathematics
Chemistry				English and American	
Botany	Psychology	Economics	Ethics		Logic
Zoology		Political Science			English
Anatomy					Foreign Language
Physiology					

In conclusion might it not be well, when we are considering fundamental changes in educational procedure to recall the thought so pithily enunciated by the versatile Goethe: "What a man inherits from his fathers he must earn for himself before he can call it his own." On occasions such as this when we gather to do honor to a group of earnest, far-sighted men who had the vision and courage in the face of difficulties to plunge boldly ahead on a course to which they had committed themselves, must we not remember that what they thought and did may only become ours as we succeed in re-envisaging their problem in a proper relationship. Advancement, then, will come to us, not by putting off the old because it is old or putting on the new because it is new, but, rather, real progress will come through a proper study and appreciation of the experience of those who have gone before, followed by a judicious interrelation and co-ordination of material. As man himself in his onward march toward greater perfection must accommodate himself to an ever-changing world, those to whom is entrusted the high responsibility of equipping pharmacists for lives of complete service must adapt themselves to the everchanging problem of education.

THE PRECIPITATING AGENTS FOR ALKALOIDS

By Charles C. Fulton

Associate Chemist, U. S. Industrial Alcohol Bureau, Minneapolis, Minn.

THE compounds known as "general alkaloidal reagents" are so called chiefly for historical reasons. They precipitate also ptomaines, proteins, basic dyes, basic nitrogenous compounds or amines in general. Some of the reagents precipitate ammonia and even the heavier alkali metals.

At first glance these reagents seem very diverse, so much so that a classification would be impossible, or at best artificial. This is not the case, however, for they may be readily divided into a few main groups. The appearance of great diversity is partly due to the fact that many possible reagents are almost unknown as such. In the following discussion I have listed, I think, at least twice as many reagents as are commonly known. A classification not only arranges the reagents that are in actual use, but also shows, in a general way, what other compounds and kinds of compounds can be used as precipitating agents. Up to the present, the discovery of new reagents seems to have been made empirically.

The alkaloids form salts, like ammonia, by addition of the acid. Their salts with the ordinary laboratory acids are generally soluble in water, while many of the free alkaloids are insoluble. Hence an alkaline reagent, or even one that merely reduces the effective acidity, may cause precipitation of the free alkaloid. Otherwise precipitation occurs when the alkaloid, acting as a base, forms an insoluble compound.

Tests can be made on an aqueous solution of the free alkaloid, when it is soluble. Occasionally precipitation tests are made on an alcoholic solution, and still more rarely on a solution with some other solvent. These precipitations are almost entirely uninvestigated.

Tests are usually made on a solution that contains the alkaloid in combination with an acid. This is obviously the most general method. For the present I shall consider only the precipitation of alkaloids from aqueous solutions of their salts, or from slightly acid solution. From such solutions the alkaloids give precipitates in the following ways:

(a) By reaction with basic reagents that free the alkaloid from its combination with acid.

(b) By combination with oxygen acids of certain elements, generally metalloids, belonging to groups 4, 5B, 6A, and 7 of the periodic table.

(c) By halogenation.

(d) By forming double or complex salts with certain metals. The metals forming such compounds belong to the B groups of the periodic table, and to group 8. The salts are halides, cyanides, thiocyanates, and nitrites.

(e) By uniting with certain organic compounds, mostly acids.

This classification may be presented as follows:

GROUP A.

I. Basic Reagents.

GROUP B. OXYGEN ACIDS.

II. Simple Oxygen Acids.
III. Complex Oxygen Acids.

GROUP C.

IV. Halogen Reagents.

GROUP D.

Double or Complex Salts with Metals.

V. Chlorides (Chloro-Acids).
VI. Bromides.
VII. Iodides.
VIII. Cyanides.
IX. Thiocyanates.
X. Nitrites.

GROUP E.

XI. Organic Reagents.

The metals of Group D in known reagents belong to the following groups of the periodic table: 1B, 2B, 4B, 5B, and 8. The subdivision of Group D may be made in this way, according to the metals of the reagents, if desired.

The simple salts, ammonium thiocyanate and potassium iodide, are, for convenience, included in Group D with the complex thiocyanates and iodides respectively, as they are hardly of sufficient importance to form a group by themselves.

Too few organic reagents are known for a subdivision of Group E.

Discussion of Reagents by Groups

All the reagents listed at the head of each of the following sections have been tested on a number of alkaloids by myself. Those marked with an asterisk were used by Stephenson, and the crystals obtained are described and many of them pictured in "Some Microchemical Tests for Alkaloids" (Lippincott, 1921).

Group A.

I. Basic Reagents.

Sodium carbonate *
Sodium hydroxide *
Sodium acetate *
Potassium chromate *
Potassium cyanide *
Ammonia
Sodium phosphate * (dibasic)
Sodium benzoate *
Sodium bicarbonate

Sodium carbonate and ammonia are sufficiently strong bases to free all alkaloids, and of course precipitate those that are insoluble. They usually have about the same effect, but the precipitate given by ammonia with quinine or quinidine will crystallize, though sodium carbonate or alkali gives only an amorphous precipitate.

Sodium (or potassium) hydroxide frees all alkaloids from combination with acid, but redissolves insoluble alkaloids that are phenols, like morphine, or those that have acid properties, like narceine. This reagent may also dissolve a precipitated alkaloid, like cocaine or heroine, by hydrolyzing it, if the test drop is allowed to stand a little while.

Sodium or potassium acetate precipitates very weak insoluble alkaloids. Sodium acetate may also be used in other cases to destroy the effective acidity for tests with certain reagents, notably tannic acid. For the latter purpose potassium acetate often cannot be used, as potassium compounds would be precipitated.

Potassium chromate is the most general and sensitive of the basic reagents toward insoluble weak alkaloids. With strong alkaloids it may, in some cases, precipitate a chromate.

Potassium cyanide, having a distinctly alkaline reaction, is effective in precipitating weak insoluble alkaloids. It also precipitates

certain alkaloids, hydrastinine, cotarnine, berberine, not precipitated by other basic reagents. This may be due to some aldehyde characteristic of these alkaloids.

Sodium phosphate has a distinctly alkaline reaction but only a small reserve of alkalinity, and is none too effective in freeing alkaloids from acid combination. It is chiefly used for its crystals with quinine. In this case there is only partial removal of the acid, quinine being dibasic.

Sodium benzoate was used by Stephenson, but seems to me an unnecessary reagent, when those already given are used. Results with it are similar to those with sodium acetate.

Sodium bicarbonate has seen some use, but is not needed.

Group B. Oxygen Acids.

II. Simple Oxygen Acids.

Ammonium Molybdate, NH_4MoO_4.*
Chromic anhydride, CrO_3.*
Potassium dichromate, $K_2Cr_2O_7$.
Perchloric acid, $HClO_4$ (or Sodium Perchlorate).
Potassium permanganate, $KMnO_4$.*

The elements of Groups 6A and 7, highly oxidized, form the simple oxygen acids that are alkaloidal precipitants. They may be used in the form of their salts. They are far inferior to the complex oxygen acids in precipitating power, but still have considerable value.

Amonium molybdate is the most general and sensitive reagent of this group. It is valuable for sensitivity determinations but gives very few crystals.

Chromic anhydride and potassium dichromate are valuable for crystals. They usually give practically the same results, but occasionally the crystals are different. Perchloric acid or sodium perchlorate is also of value for crystals.

Potassium permanganate because of its great oxidizing power and its deep color is not of much value as a general reagent. It is chiefly of use in identifying the few alkaloids, such as aconitine and cocaine, that yield fairly stable crystalline permanganates. Results, at least with the two alkaloids mentioned, are best in acidified solution, and perhaps the reagent should be called permanganic acid for preference.

III. Complex Oxygen Acids.

Phosphomolybdic acid.*
Phosphotungstic acid.*
Silicotungstic acid.*
Arsenitungstic acid.
Sodium phosphomolybdate.*

The complex oxygen acids of such elements as phosphorus, arsenic, antimony, molybdenum, tungsten and silicon (metalloids of Groups 4, 5B and 6A) have the most general action of all the reagents. Besides those listed above, phosphoantimonic acid (Schulze's reagent) and arsenimolybdic acid [1] have been used.

Phosphomolybdic and phosphotungstic acids are the principal reagents of the class. They precipitate all alkaloids from aqueous solution. They also precipitate alkaloids from alcohol, and are useful in testing special denatured alcohol.

Reagents of this class as a rule give crystals only with rather simple basic compounds. With the majority of the alkaloids they give only amorphous precipitates.

These reagents do not have such a general action in the form of their salts. Sodium phosphomolybdate precipitates only about half the alkaloids.

Group C.

IV. Halogen Reagents.

Bromine water.
Bromine in sodium bromide. Bromine in hydrobromic acid.
Iodine water.
Iodine in sodium bromide.
Wagner's reagent, or iodine in potassium iodide solution. (A number of forms of the reagent are possible.) (* One form only used by Stephenson.)
Iodine in hydriodic acid.
Iodine-zinc-chlor-iodide.*
Kraut's reagent * (contains iodine soon, though not when first made).

Chlorine has practically no value as an alkaloidal precipitant, but both bromine and iodine are much used.

[1] Sterkin and Helfgat. Biochem. Z. 207, 8 (1929). Chem. Ab. 23, 3050.

Bromine water is a very general precipitant, but gives crystals as a rule only with rather simple bases. Most of the alkaloids give amorphous precipitates, and for this reason the reagent was discarded by Stephenson. However it gives useful crystals with atropine and allied alkaloids. In using bromine it should be remembered that it is also a phenol precipitant, and an oxidizing agent.

Bromine in NaBr is more sensitive to many simple bases than bromine water. The maximum sensitivity to simple alkaloids that are very weak bases, as caffeine, for example, is obtained by using bromine in hydrobromic acid. This is sometimes called Wormley's reagent.[2] The guess in "Allen's" that bromine in strong hydrochloric acid would be equally effective [3] happens not to be correct.

Iodine water, when fresh, is not a sensitive reagent, and is practically worthless, generally giving amorphous precipitates, though narceine gives crystals. When aged for several days, or longer, it has the same action as a very weak solution of hydriodic acid saturated with iodine.

The use of sodium bromide solution to dissolve iodine provides a convenient means of preparing a weak iodine solution of more definite strength than aged iodine water, and having a similar action.

The outstanding reagent of the group is Wagner's, or iodine in potassium iodide solution. A number of different forms of this reagent are of value. With atropine, for example, some four different types of crystals may be obtained by altering the ratio of potassium iodide to iodine in the reagent.[4] Many alkaloids give at least two different kinds of crystals with different proportions of potassium iodide. Variation of the potassium iodide also affects the sensitivity to many alkaloids. This phenomenon is of great assistance in classifying the alkaloids.[5] The reagent saturated with iodine is the most sensitive. Bases like ephedrine, arecoline, and scopolamine show a noticeable decline in sensitivity with a small excess of potassium iodide, and a continued steady decline as the potassium iodide is increased. The sensitivity toward atropine, codeine, etc., is scarcely

[2] Wormley: Microchemistry of Poisons (Bailliere, 1867).

[3] Allen's Commercial Organic Analysis, vol. VI, page 189. (Blakiston, 1912.)

[4] Fulton: The Identification of Atropine with Wagner's Reagent. Jour. A. O. A. C., vol. XII, p. 312 (1929).

[5] Fulton: The Identification of Alkaloids by Precipitation. I. A Natural Classification of the Alkaloids Based on Precipitation. Jour. A. O. A. C, XIII, p. 491 (1930).

affected by a little potassium iodide, but is notably reduced by a large amount. Cocaine, quinine, strychnine, etc., show little change in sensitivity no matter how much potassium iodide is added.

Wagner's reagent may be acidified. It is given by Blyth as iodine in hydriodic acid.[6] The results obtained in an acid test drop or with an acid reagent may be quite different from those given by the neutral reagent, especially if the solution tested contains the free base. Simple very weak bases, as caffeine, ecgonine and antipyrine, require strong acidification of the test drop for sensitivity; in fact caffeine is not precipitated at all by the neutral reagent. With ammonia the contrary is true; as the free base it is precipitated, but from compounds with acids it is not. Hexamethylenetetramine gives different crystals in the two cases. Morphine crystals are most readily formed when a little acid in excess of that combining with the alkaloid is present. Certain pseudomorphine crystals require excess acid. Sulphuric acid is needed for crystallization with quinine and quinidine, herapathite crystals being formed. Probably there are some other cases where a particular acid is necessary.

Forms of the reagent strongly acidified with sulphuric acid, others weakly acidified with acetic acid, are useful for tests. The acid reagents will not keep indefinitely, however, and are best prepared as needed from the neutral forms.

Stephenson used two iodine reagents besides Wagner's: "Zinc-chlor-iodide" and Kraut's reagent.

"Zinc-chlor-iodide" as used by Stephenson consisted of a very concentrated zinc chloride solution with potassium iodide and iodine added. Such a solution is used for staining vegetable products for microscopical study.[7] Some authorities use for the alkaloidal precipitant a much less concentrated solution of zinc chloride and potassium iodide, omitting the iodine.[8] (See discussion of iodide reagents.) It is doubtful if the iodine serves any purpose except to produce certain crystals that could be obtained with some form of Wagner's reagent.

Kraut's reagent is a form of Dragendorff's, or bismuth-potassium-iodide, but the nitric acid and potassium iodide in it react before

[6] Blyth: Poisons, Their Effects and Detection, ed. 5, p. 250. (Griffin, 1920.)

[7] Leach and Winton: Food Inspection and Analysis, ed. 4, p. 78. (Wiley, 1920.)

[8] Autenrieth-Warren: Detection of Poisons, ed. 5, p. 319. (Blakiston, 1921.)

long to give iodine. The reagent then acts like a mixture of Dragendorff's reagent with Wagner's. In discussing twenty-six crystalline precipitates with Kraut's reagent, Stephenson states specifically in nine cases that the crystals are the same as those given by Wagner's reagent. The bismuth-potassium-iodide reagent should be made up in a more stable form than that given by Kraut's formula, and should be kept distinct from Wagner's reagent.

GROUP D.

Double or Complex Salts with Metals.

V. Chlorides or Chloro-Acids.

(a) Stable chloro-acids.

Chlor-auric acid, $HAuCl_4$.*
Chloro-platinic acid, H_2PtCl_6.*
Chloro-palladous acid ($PdCl_2$ in dilute HCl).*
Chloro-mercuric acid (probably $HHgCl_3$).
Sodium mercuric chloride (probably $NaHgCl_3$).
Other forms of the mercuric chloride reagent, with excess HCl or NaCl, are possible.

(b) Chlorides requiring an excess of hydrochloric acid to prevent basic hydrolysis or to form the chloro-acid.

Bismuth chloride in HCl.
Antimony chloride in HCl.
Stannous chloride in HCl.
Stannic chloride in HCl.
Ferric chloride in HCl.
Zinc chloride in HCl.
Cadmium chloride in HCl.
(The HCl is fully concentrated only in the $FeCl_3$ reagent.)

(c) Simple chlorides.

Mercuric chloride.*
Cadmium chloride.
Zinc chloride.*
Ferric chloride.*

Members of this group are usually referred to as though simple chlorides, but the actual precipitating agents are nearly always chloro-acids or double chlorides. The outstanding reagents, commonly called

"gold chloride" and "platinum chloride," are of course actually chlor-auric acid, $HAuCl_4$, and chloro-platinic acid, H_2PtCl_6. Palladous chloride is used in dilute hydrochloric acid and in all probability H_2PdCl_4 is the actual precipitating agent. Stephenson used simple mercuric chloride, but usually in conjunction with the hydrochloride of the alkaloid. When the alkaloid is in the form of the sulphate, phosphate, acetate, or the like, simple $HgCl_2$ usually lacks sensitivity and sometimes even fails to precipitate at all. For sensitivity, and as a standard reagent, the mercuric chloride reagent should be prepared with exactly the right proportion of hydrochloric acid or sodium chloride.

With these stable chloro-acids an excess of hydrochloric acid or sodium chloride has some solvent effect on the precipitate, quite marked in the case of the mercuric reagents. Excess chloride may also induce or aid crystallization, or change the shape of the crystals. Stephenson mentions that the precipitate of cocaine with palladous chloride crystallizes much more quickly if some chlorine or hydrochloric acid is added. Similarly pseudomorphine in acetic acid solution requires extra chloride for crystals with the same reagent. Quinine with mercuric chloride crystallizes most readily when a large excess of hydrochloric acid is present, and these crystals are very characteristic.

Somewhat different are the reagents that require the presence of strong hydrochloric acid. In the case of bismuth and antimony the chloro-acids are probably as stable as the chlorides, but considerable excess hydrochloric acid is necessary to prevent hydrolysis to insoluble basic compounds. Stannous chloride, stannic chloride, and ferric chloride require strong hydrochloric acid for sensitivity, probably because the chloro-acids are decomposed by water. The use of stannous chloride and ferric chloride in concentrated hydrochloric acid was recommended long ago by Godeffroy. Zinc and cadmium can be used almost as well as simple chlorides, but are somewhat more sensitive in the presence of fairly strong hydrochloric acid.

Both chlorides of lead have been used as alkaloidal precipitants,[9] but it is doubtful if either of these reagents has much value.

[9] Witthaus: Manual of Toxicology, ed. 2, p. 172. (Wood, 1911.) $PbCl_2$. Arreguine and Amadeo: Lead Tetrachloride as a Reagent for Alkaloids, etc. Semana med. 36, 645 (1929). Chem. Ab. 23, 5272.

As to simple chlorides, only those of zinc, cadmium and mercury deserve places amongst the reagents. Aqueous ferric chloride solution was used by Stephenson but has little precipitating power: ferric chloride in concentrated HCl should be used. When tests are made with simple mercuric chloride the use of the alkaloidal hydrochloride should be avoided and care should be taken that no halogen acid is present, in order that results with the simple chloride may not be confused with those given by the chloro-acid or sodium mercuric chloride.

VI. Bromides.

Mercuric sodium bromide.
Bromo-platinic acid.
Bromo-bismuth acid (bismuth bromide in HBr).
Cadmium sodium bromide.
Brom-auric acid.
Ferric bromide in HBr.

Probably all the metals that are useful as chlorides can be used as bromides. Bromide reagents have not seen much use, however. None were used by Stephenson. Intermediate between the chlorides and the iodides, and generally similar to the chlorides, there is no great necessity for some of them. Some, however, are of considerable value.

Of these reagents only mercuric potassium bromide has seen any real service,[10] although potassium bromide or sodium bromide is occasionally added to the test drop after gold chloride or other chloride reagent.

Bromo-platinic acid will unquestionably prove a very important and useful reagent. With cinchonine it readily gives beautiful and characteristic crystals, although the precipitate with chloro-platinic acid will scarcely crystallize at all, even when excess chloride is present.

Brom-auric acid gives practically the same results as chlor-auric with most alkaloids, but is a little more sensitive toward the simpler bases. Toward ecgonine brom-auric acid is much more sensitive than chlor-auric, and provides what is probably the best microchemical test for ecgonine.

[10] Rosenthaler: Microchemical Characterization of Drugs. Am. Jour Pharm. 100, 757 (1928).

Zinc sodium bromide seems unnecessary, as in the case of zinc the chloride and iodide reagents are similar. An antimony bromide reagent is probably unnecessary, as the antimony compounds closely resemble those of bismuth. Ferric bromide in hydrobromic acid seems to be closely similar to ferric chloride in hydrochloric acid.

VII. Iodides.

Mayer's reagent.*
Mayer's & KI.
Marme's reagent.*
Cadmium iodide.
Zinc potassium iodide (zinc-chlor-iodide, with iodine *).
Dragendorff's reagent (Kraut's reagent).*
Antimony potassium iodide.
Stannous sodium iodide.
Potassium iodide.*
Platinum iodide & NaI.
Silver sodium iodide.
Lead sodium iodide.

The more sensitive iodide reagents are among the most general and sensitive of all the alkaloidal reagents. They surpass all except the complex oxygen acids and the halogen reagents in precipitating power. They are also of great value for crystals.

With Mayer's reagent, or mercuric potassium iodide, even more than with Wagner's, an excess of potassium iodide (more than enough to hold the HgI_2 in solution) greatly reduces the sensitivity to certain alkaloids, and may also result in a different type of crystals. The concentration of the reagent may also influence the crystallization, as well as the sensitivity toward simple bases. Three types of crystals are given by morphine and different forms of the reagent. Mayer's reagent must be very strongly acidified to precipitate caffeine and similar very weak bases; in fact such strong acidification is needed that the fact of precipitation has been overlooked, and texts generally state that caffeine is not precipitated by Mayer's reagent.[11]

Dragendorff's reagent, or bismuth potassium iodide, may also be used in several forms: with excess potassium iodide, or with very strong acidification, etc. In this case the standard reagent has to be

[11] For instance: Fuller: Chemistry and Analysis of Drugs and Medicines, p. 288. (Wiley, 1920.)

decidedly acid to prevent basic hydrolysis. The iodide reagents of bismuth, antimony, and tin, since they must be acid, decompose more or less rapidly, iodine being formed from the hydriodic acid. Dragendorff's reagent, if made with sulphuric rather than nitric acid, will keep in fair condition for several months. The antimony and stannous iodide reagents have to be made up fresh.

With Marme's reagent, cadmium potassium iodide, the proportion of potassium iodide has very little effect. A simple solution of cadmium iodide gives similar results. Zinc iodide can also be used instead of zinc potassium iodide, without any great loss of precipitating power.

Simple potassium iodide is used to some extent as an alkaloidal reagent, but it is not very sensitive, and scarcely comparable to the double and complex iodides.

Silver sodium iodide and lead sodium iodide require strongly concentrated sodium iodide solutions to hold the AgI and PbI_2 in solution.

VIII. Cyanides.

Potassium ferrocyanide.*
Potassium ferricyanide.*
Sodium nitroprusside (sodium nitroferricyanide).*
Platinum cyanide reagent.
Gold cyanide reagent.

Only those complex cyanides that are fairly stable in acid solution can be used, because complexes formed by adding potassium cyanide to neutral salts, as well as potassium cyanide itself, act as basic reagents. The only cyanide reagents to which I have ever seen any references are the first three given above. My own observations indicate that the platinum and gold cyanide reagents will be of great value.

IX. Thiocyanates.

Platinum sodium thiocyanate.
Mercuric potassium thiocyanate.
Zinc sodium thiocyanate.
Cobalt sodium thiocyanate.
Cadmium sodium thiocyanate.
Ferric sodium thiocyanate.
Stannous sodium thiocyanate.

Nickel sodium thiocyanate.
Manganous sodium thiocyanate.
Ammonium thiocyanate.*

This is a neglected group. Only ammonium thiocyanate was used by Stephenson, and the double thiocyanates are not in common use, despite the fact that the platinum, mercuric and zinc thiocyanate reagents are all more sensitive and general than Marme's reagent. The cobalt, cadmium, ferric and stannous thiocyanate reagents are also good precipitating agents. For some reason I cannot explain cadmium sodium thiocyanate is less sensitive than zinc sodium thiocyanate and also less sensitive than cadmium potassium iodide. Ferric sodium thiocyanate readily precipitates alkaloids, but is so deep a color as not to make a very desirable reagent.

Nickel sodium thiocyanate, though a desirable reagent, is not nearly so sensitive as those mentioned in the preceding paragraph. Manganous sodium thiocyanate seems nearly on a par with it, even though manganese is not a B group metal. However, neither the nickel nor manganese reagent is very much superior to simple sodium or ammonium thiocyanate.

Bismuth seems not to form a practicable thiocyanate reagent; but stannous sodium thiocyanate is available, if made up fresh when wanted. Copper, silver and gold thiocyanates are insoluble; the cupric and auric thiocyanates somewhat unstable too.

Reinecke's salt, $NH_4(NH_3)_2Cr(SCN)_4$, has been recommended by a number of authorities as an alkaloidal precipitant, but I have never tried it.

The double thiocyanates are but slightly affected by excess of thiocyanate. They usually give amorphous precipitates, but some valuable crystals are known.

X. Nitrites.

Mercuric sodium nitrate.
Mercuric sodium chloro-nitrite.
Millon's reagent.*
Sodium cobaltic nitrite.
Lead copper sodium nitrite.
Lead sodium nitrite.

Mercuric sodium nitrite is the most valuable reagent of this group. I have never seen it mentioned as an alkaloidal precipitant,

but Millon's reagent probably owes whatever specific value as a precipitant it possesses to the presence in it of a mercuric nitrite compound.

Millon's reagent is made by dissolving mercury in nitric acid and contains mercuric and mercurous nitrates and nitrites. The nitrates are not effective as alkaloidal precipitants. The reagent is a poor one, as it precipitates mercurous chloride from alkaloidal hydrochloride solutions, and may precipitate mercuric sulphate from alkaloidal sulphate solutions, and in addition it will not withstand much dilution, but gives a precipitate merely by the addition of water. Stephenson obtained some alkaloidal precipitates with the reagent which were probably double chlorides or bromides, due to using the hydrochlorides of the alkaloids in most cases and the hydrobromides in a few. Mercuric sodium nitrite is not a particularly sensitive reagent.

It may be mentioned here that there is no class of nitrate reagents, although Stephenson used silver nitrate and barium nitrate as well as Millon's reagent. Most of the precipitates he obtained were silver chloride or silver bromide or barium sulphate.

Sodium cobaltic nitrite and lead copper sodium nitrite, well known as precipitants of potassium, have been used occasionally to precipitate the alkaloids. They are not particularly sensitive. Rosenthaler also used $K(NH_3)_2Co(NO_2)_4$.[12]

The following table for Group D shows the known reagents obtained by combining the various metals and anions:

	Copper	Silver	Gold	Zinc	Cadmium	Mercury	Tin	Lead	Antimony	Bismuth	Iron	Cobalt	Nickel	Platinum	Palladium	Manganese
Chloride			R	R	R	R	2R	2r	R	R	R			R	R	
Bromide			R	r	R	R	r	r	r	R	r			R		
Iodide		R		R	R	R	R	R	R	R				R		
Cyanide			R								3R			R		
Thiocyanate				R	R	R	R				R	R	R	R		R
Nitrite	R*					R		2R*				R				

R = reagent known and tested. r = reagent reported, or obviously practicable, but not sufficiently tested in this study. The numeral

[12] Rosenthaler: Microchemical Reagents for Alkaloids. Sweiz. Apoth. Ztg. 61, 118 (1923). Chem. Ab. 17, 2171.

2 or 3 indicates that two or three reagents are known containing the same metal and anion. *, one nitrite reagent requires both copper and lead.

Some of the blank spaces in the above table can be filled in as new reagents are discovered by further research; others, because of the formation of insoluble, unstable or completely ineffective compounds, never can be. Palladium compounds corresponding to those of platinum can no doubt be made, but they would be of extremely deep color, making them of limited value. It is doubtful if copper, nickel, or manganese can be used to make any really effective reagent. A few tests were made on arsenic: it appears to be too feebly basic to make any reagent.

Group D can be extended beyond the limits of the above table. For instance, selenocyanates might be used. This has never been done in testing alkaloids, so far as I know, but derivatives of aniline and pyridine with cobalt, nickel, or cadmium salts and KSeCN have been formed.[13] Cyanate has been similarly used.[14] It is doubtful if cyanate reagents would be sufficiently stable for use in acidified solutions, but they might be used in testing free alkaloids. It is difficult to define the precise limits of Group D. I know of no text that states what anions are like the halides in forming double salts of the type effective as alkaloidal precipitants.

Group E.

XI. Organic Reagents.

Picric acid.*

Tannic acid.

Sodium tannate (tannic acid with sodium acetate or sodium carbonate).

Saccharin or sodium saccharate.*

Sodium alizarin sulphonate.

The organic reagents offer quite a field for investigation, as it can hardly be supposed that the above list exhausts the useful reagents.

Stephenson used picric acid and saccharin, or rather sodium saccharate, since the saccharin is brought into solution by sodium hydroxide. He also tried tannic acid, but discarded it.

[13] Spacu and Macarovici: A New Class of Ammines—the Selenocyanammines. Bul. Soc. stiinte Cluj 5, 169 (1930). Chem. Ab. 24, 4231.

[14] Ripan: Bul. soc. stiinte Cluj. 4, 144 (1928). Chem. Ab. 23, 2905.

Picric acid is a very valuable reagent both for sensitivity and crystals. Saccharin is not very sensitive. Tannic acid and sodium tannate apparently give no crystals. Tannic acid, in acid solution, is not very sensitive. Some authorities say that it should be applied to neutral or faintly alkaline solution; some combine it with sodium acetate or sodium carbonate. A sodium tannate reagent can have some use for sensitivity determinations. Tannic acid (or sodium tannate) is a long known reagent, and is nearly always given in the texts as one of some half-dozen traditional alkaloidal reagents, but it could be discarded without much loss.

Tri-nitro-resorcin has been used occasionally to precipitate alkaloids. It seems to give results closely similar to those with picric acid. Other nitro-phenols have also been used.[15]

Picrolonic acid has had considerable use, but chiefly in alcoholic solution, and for melting point tests.[16] Picric acid is also used in this way.

With sodium alizarin sulphonate, used by Rosenthaler,[17] I have made only a few tests to date. It appears to be a valuable reagent. The sulphonic acid and other derivatives of anthraquinone have also been used.[18]

Trichloracetic acid precipitates proteins, and will precipitate a few alkaloids, but according to my observations is not sensitive to any alkaloid. Xanthates have been given as alkaloidal reagents.[19]

A few other organic reagents have been suggested for the precipitation of particular alkaloids, but they have seen little, if any, general use.

Ninety-one Reagent Formulas

Surprisingly little attention has been given to the question of the proper formulas for the reagents. The formulas in the texts at present are largely traditional, and can often be improved on. In gen-

[15] Rosenthaler and Goerner: Aromatic Nitro-Derivatives, Especially Nitrophenols, as Alkaloidal Precipitants. Z. anal. Chem. 49, 340. Chem. Ab. 5, 1159.

[16] Mulliken: Identification of Pure Organic Compounds, vol. II, p. 33. (Wiley, 1916.)

[17] Rosenthaler: Sodium Alizarin Sulphonate as a Reagent for Alkaloids. Apoth. Ztg. 45, 638 (1930). Chem. Ab. 24, 3858.

[18] Zimmermann: Anthraquinone Derivatives as Precipitants for Bases. Z. physiol. Chem. 192, 124 (1930). Chem. Ab. 25, 101.

[19] Navarro: Alkali Xanthates as Reagents for Alkaloids. Anales soc. espan. fis. Quim. 24, 125 (1925). Chem. Ab. 20, 2227.

eral the most sensitive form of the reagent should be taken as the standard. Other forms are often desirable for crystal tests, or for comparison of the sensitivity with the standard reagent. The concentration of a reagent should be great enough that an increase in concentration will not markedly increase the sensitivity of the reagent to common alkaloids.

The following reagents should be used, in general, by adding one full drop of reagent, letting it fall from a 1 cc. pipette into a drop of the alkaloidal solution of equal or somewhat greater size. Three such tests can be made on the ordinary microscope slide. This procedure should be uniformly followed for sensitivity tests, as it is then necessary to add the same quantity of reagent each time, and to have the reagent in excess. In obtaining crystals, however, it may sometimes be desirable to put a drop of reagent beside a drop of the alkaloidal solution, and allow the two drops to flow into each other; or to use a minimum of reagent, adding only a very small drop on the end of a glass rod.

I. Basic Reagents.

(1) *Sodium carbonate.* A 5 per cent. solution of Na_2CO_3.

(2) *Ammonia.* A 5 per cent. solution of NH_4OH.

(3) *Alkali.* A 5 per cent. solution of NaOH or KOH.

(4) *Potassium chromate.* A 5 per cent. solution of K_2CrO_4.

(5) *Sodium acetate.* A 5 per cent. solution. (For crystals and for destroying acidity.)

(6) *Concentrated potassium acetate.* Thirty gm. in 100 cc. water. (For sensitivity and crystals.) Concentrated sodium acetate could be used.

(7) *Potassium cyanide.* A 5 per cent. solution of KCN, freshly prepared.

(8) *Sodium phosphate (dibasic).* A 5 per cent. solution of Na_2HPO_4.

II. Simple Oxygen Acids.

(9) *Ammonium molybdate.* A 5 per cent. solution of NH_4MoO_4.

(10) *Chromic anhydride.* A 5 per cent. solution of CrO_3.

(11) *Potassium dichromate.* A 5 per cent. solution of $K_2Cr_2O_7$.

(12) *Perchloric acid.* A 5 per cent. solution of $HClO_4$.

(13) *Potassium permanganate or permanganic acid.* A 5 per cent. solution of $KMnO_4$ acidified with a few drops per 100 cc. of 85 per cent. H_3PO_4. Use only a small drop of this reagent, added on the end of a glass rod.

III. Complex Oxygen Acids.

(14) *Phosphomolybdic acid.* A 10 per cent. solution of phosphomolybdic acid crystals. If the solution is to be kept a considerable time 1 per cent. of concentrated HNO_3 should be added to prevent hydrolysis, at least if the crystals and solution are green-yellow rather than golden-yellow.

(15) *Phosphotungstic acid.* A 10 per cent. solution.

(16) *Silicotungstic acid.* A 10 per cent. solution.

(17) *Sodium phosphomolybdate.* (a) A 10 per cent. solution. (b) Neutralize a 10 per cent. solution of phosphomolybdic acid with sodium hydroxide. This reagent is colorless while the acid is yellow or green-yellow.

IV. Halogen Reagents.

(18) *Bromine water.* A saturated aqueous solution of bromine.

(19) *Bromine in NaBr.* A 5 per cent. solution of NaBr saturated with bromine. (About 4 cc. of Br required.)

(20) *Bromine in HBr.* NaBr — 5 gm., water — 90 cc., H_2SO_4 (1 + 3) — 10 cc. Saturate with bromine.

It may seem like splitting hairs to have eight varieties of Wagner's reagent differing only in the proportion of potassium iodide. However no other reagent is so well suited for determining the decline of sensitivity shown by many alkaloids with an excess of potassium iodide, although Mayer's reagent can also be used for this purpose. In addition, characteristic crystal tests often require a particular ratio of iodine to potassium iodide within such narrow limits as to justify at least five of these reagents by the cases known at present. Some of these cases are mentioned in connection with the formulas:

(21) *Wagner's No. 1.* Saturated or standard form. Dissolve 1 gm. KI and 1 gm. iodine completely in about 1 cc. water, add a few more iodine crystals, then dilute gradually, or with lukewarm water (to avoid cooling by dilution of the KI solution) to 100 cc. A little iodine is precipitated as a result of the dilution. This is the most

sensitive form of the reagent. (Rod crystals with dilute solutions of Scopolamine. Rods with homatropine.)

(22) *Wagner's No. 2.* Dissolve 1 gm. iodine and 1.75 gm. KI in 2 cc. water, then add 98 cc. water.

(23) *Wagner's No. 3.* Dissolve 1 gm. iodine and 2.75 gm. KI in 3 cc. water, then add 97 cc. water. (Rod crystals with dilute solutions of atropine.)

(24) *Wagner's No. 4.* Dissolve 1 gm. iodine and 5 gm. KI in 10 or 15 cc. water, then add the balance of 100 cc. water. This is the "Wagner's reagent" used by Stephenson, and the form for which the greatest number of crystals have been described and illustrated.

(25) *Wagner's No. 5.* Iodine—1 gm., KI—10 gm., water—100 cc. (Small yellow plates with atropine.)

(26) *Wagner's No. 6.* Iodine—1 gm., KI—20 gm., water—100 cc.

(27) *Wagner's No. 7.* Iodine—1 gm., KI—35 gm., water—100 cc. (This or the preceding reagent gives the most ready crystallization with pilocarpine or moderately concentrated solutions of scopolamine.)

(28) *Wagner's No. 8.* Iodine—1 gm., KI—50 gm., water—100 cc. (Orange-red hexagonal plates with atropine. Black rosettes with pseudomorphine.)

Each of the first seven forms of Wagner's reagent, tested with scopolamine, ephedrine, or arecoline, is approximately twice as sensitive as the next following form of the reagent.

Occasionally characteristic crystals may form most readily with even more than fifty times as much potassium iodide as iodine, by weight. Thus far, however, pseudomorphine is the only alkaloid I have found with which this is the case.

(29) *Acid Wagner's.* A strongly acid variety of any of the above forms of Wagner's reagent (for the precipitation of very weak bases) is made by adding to 9 cc. of the neutral reagent 1 cc. of (1 + 3) H_2SO_4. If only a slightly acid test drop, to insure the combination of a strong alkaloid, is required, a little acetic acid will suffice. Acid forms of Wagner's reagent will not keep.

(30) *Iodine in NaBr.* Dissolve 2 gm. NaBr in 100 cc. water and add iodine crystals. Let stand, with occasional shaking, for at least an hour or two before use.

An acid form of this reagent may also be made by adding to 9 cc. 1 cc. of (1 + 3) H_2SO_4.

If any form of this reagent with excess NaBr is made, it should not contain over 0.25 gm. iodine.

V. Chlorides.

(31) *Chlor-auric acid or "gold chloride."* A 5 per cent. solution of $HAuCl_4.4H_2O$ crystals.

(32) *Chloro-platinic acid or "platinum chloride."* A 5 per cent. solution of $H_2PtCl_6.6H_2O$ crystals.

(33) *Chloro-palladous acid or "palladium chloride."* Dissolve 5 gm. $PdCl_2$ in 95 cc. water and 5 cc. conc HCl. $PdCl_2$ dissolves very incompletely in plain water, due to the formation of a basic salt.

(34) *Chloro-mercuric acid.* $HgCl_2$—5 gm., conc HCl—1 cc., water—100 cc. This is the most sensitive acid form of the mercuric chloride reagent. The HCl may be varied from about 0.75 cc. to about 1.50 cc. The upper limit corresponds to $HHgCl_3$, and this is probably the precipitating agent.

(35) *Mercuric sodium chloride.* $HgCl_2$—5 gm., NaCl—0.75 gm., water—100 cc. This is the most sensitive form of the mercuric chloride reagent, the neutral reagent being somewhat more sensitive than the acid. The NaCl may be varied from 0.5 to 1.0 gm. (limits empirically determined). The precipitating agent is probably $NaHgCl_3$.

Since the quantities of NaCl and HCl in this and the preceding reagent are small, a little acid in the test drop will convert this reagent into the preceding one, chloro-mercuric acid. Hence for sensitivity determinations a "neutralizing form" of this reagent is used. To the formula add sodium acetate—10 gm.: this gives *mercuric sodium chloride, neutralizing form.*

(36) *Mercuric chloride & HCl.* $HgCl_2$—5 gm., conc HCl—15 cc., water—85 cc. This formula is more or less tentative, as I have not yet found a definite basis for determining exactly how much HCl should be present for this type of reagent.

(37) *Mercuric chloride & NaCl.* $HgCl_2$—5 gm., NaCl—25 gm., water—100 cc. This formula is also somewhat tentative. For a neutralizing form add sodium acetate—10 gm.

(38) *Simple Mercuric Chloride.* A 5 per cent. solution of $HgCl_2$. If the characteristic results of this reagent are to be ob-

served, entirely distinct from those of chloro-mercuric acid or mercuric sodium chloride, it must not be used with hydrochlorides or hydrobromides of the alkaloids (nor in solutions containing halides), but only with alkaloidal sulphates, phosphates, acetates, or the like.

(39) *Cadmium chloride.* A 5 per cent. solution of $CdCl_2$.

Cadmium chloride in HCl. $CdCl_2$—5 gm., conc HCl—10 cc., water—90 cc. The alkaloids thus far tested show such slight changes in sensitivity with change in the HCl content that it is little more than a guess to say that 10 cc. HCl gives the most sensitive form. There is no great difference between the reagent with HCl and simple $CdCl_2$.

(40) *Zinc chloride.* A 5 per cent. solution of $ZnCl_2$.

Zinc chloride in HCl. $ZnCl_2$—5 gm., conc HCl—40 cc., water—60 cc. The sensitivity varies only slightly if the HCl content is halved or doubled, and the sensitivity of the reagent with HCl is not a great deal above that of simple $ZnCl_2$.

(41) *Bismuth chloride in HCl.* Bismuth subnitrate—5 gm., water—75 cc., conc HCl—25 cc.

(42) *Antimony chloride in HCl.* $SbCl_3$—5 gm., water—50 cc., conc HCl—50 cc.

The above two reagents require the specified amounts of HCl to prevent precipitation of BiOCl or SbOCl in the test drop. More HCl reduces the sensitivity.

(43) *Stannic chloride in HCl.* Treat 5 gm. tin with 80 cc. conc HCl. When the evolution of hydrogen slackens, warm on the water bath to dissolve the last of the tin. Add 1 or 2 cc. conc HNO_3. The solution becomes yellow. Add 20 cc. water.

The proportion of HCl in this reagent may be varied from two-thirds to the entire omission of water. Crystals seem to be better if the water is not entirely omitted. If the nitric acid is omitted the $SnCl_2$ will gradually go over to $SnCl_4$ anyway. $SnCl_4$ has a yellow color in concentrated HCl, while $SnCl_2$ has a weak blue color.

(44) *Stannous chloride in HCl.* Treat 7 gm. tin with 40 cc. conc HCl in the cold. When hydrogen is no longer noticeably evolved add 60 cc. water and an additional 3 gm. of tin.

About 40 cc. of HCl (or more) is desirable for sensitivity; 20 or 25 cc. would suffice to dissolve the tin and hold the $SnCl_2$ in solution.

(45) *Ferric chloride in HCl.* $FeCl_3$—10 gm., conc HCl—100 cc. 10 gm. $FeCl_3$ rather than 5 are necessary for sensitivity. When only 5 gm. $FeCl_3$ are used one notices that the sensitivity is increased by adding two drops of reagent instead of one. Concentrated HCl is required for sensitivity.

VI. Bromides.

(46) *Mercuric sodium bromide.* Dissolve 2 gm. NaBr in 100 cc. water and add $HgBr_2$ to saturation. (About 5 gm. $HgBr_2$ required.) Excess of NaBr over that required to dissolve the $HgBr_2$ will diminish the sensitivity.

Or, dissolve 5 gm. $Hg(NO_3)_2$ in 50 cc. water with the addition of just enough HNO_3 to give a clear solution. Add 10 per cent. NaBr solution until the precipitated $HgBr_2$ just dissolves. This requires a little less than 50 cc. of NaBr solution. Make up to 100 cc. with water. The precipitating agent would seem to be $NaHgBr_3$.

(47) *Mercuric sodium chloro-bromide.* $HgCl_2$—5 gm., NaBr—4 gm., water—100 cc. This is the most sensitive form of mercuric bromide reagent that can be prepared from mercuric chloride. It would seem to be a solution of $HgBr_2$ in NaCl, or $NaHgClBr_2$. Its sensitivity is practically the same as that of mercuric sodium bromide but its crystals are sometimes noticeably different.

(48) *Bromo-platinic acid.* H_2PtCl_6 crystals—5 gm., NaBr—6 gm., water—100 cc. Heat the solution for a short time on the water bath. It becomes orange-red.

(49) *Brom-auric acid.* $HAuCl_4$ crystals—5 gm., NaBr—5 gm., water—100 cc. The reagent is deep red. Its reactions in most cases are closely similar to those of chlor-auric acid. Excess of NaBr has little or no effect.

(50) *Bromo-bismuth acid or bismuth bromide in HBr.* Bismuth subnitrate—5 gm., NaBr—15 gm., water—60 cc., H_2SO_4 (1 + 3)—40 cc. Both acid and NaBr are needed to hold $BiBr_3$ in solution, and an excess of one or the other must be present to prevent precipitation in the test drop. The above formula contains an excess of both.

(51) *Cadmium sodium bromide.* $CdCl_2$—5 gm., NaBr—15 gm., water—100 cc. More NaBr seems to have no solvent action, but only a slight salting-out effect.

VII. Iodides.

(52) *Mayer's reagent* (*mercuric potassium iodide*). Dissolve 2 gm. KI in 100 cc. water and saturate with HgI_2. (This requires nearly 3 gm. HgI_2.) Leave a little undissolved HgI_2 in contact with the solution.

(53) *Concentrated Mayer's reagent.* Dissolve 10 gm. KI in 100 cc. water and saturate with HgI_2 (about 15 gm. required). This reagent shows a greater sensitivity to simple bases than the standard form, and may give different crystals. It is also used to prepare a strongly acid reagent (the one following).

(54) *Acid Mayer's reagent.* To 2 cc. of the above concentrated Mayer's reagent add 4 cc. water and 4 cc. of (1 + 3) H_2SO_4. Filter off the precipitated HgI_2. This reagent is used for the precipitation of simple very weak bases. To insure an acid test drop with strong alkaloids a little acetic acid will do.

(55) *Mayer's & KI.* HgI_2—3 gm., KI—15 gm., water—100 cc. This formula was originally decided on by observations on the crystals of morphine and (more especially) codeine, but the reagent has since proved of great value for sensitivity determinations. It has many points of similarity to Marme's reagent. In sensitivity it has about the same relation to Mayer's reagent that Wagner's No. 8 does to Wagner's No. 1.

(56) *Marme's reagent.* CdI_2—5 gm., KI—4½ gm., water—100 cc. The formula corresponds to K_2CdI4 and any great variation from the proportion of the iodides given makes a less sensitive form, but the KI may be varied from 4 to 7½ gm. (with 5 gm. CdI_2) with scarcely any noticeable change in sensitivity. The formula usually given for Marme's reagent is more concentrated and has more potassium iodide in proportion than the one given here.

Simple cadmium iodide, in 5 per cent. solution, may be used. The results are so similar that it may be regarded as merely a less sensitive form of Marme's reagent.

(57) *Zinc potassium iodide.* Zinc acetate—5 gm., KI—20 gm., water—100 cc. The precipitating agent seems to be K_2ZnI_4, but an excess of KI has only a slight salting-out effect.

(58) *Silver sodium iodide.* $AgNO_3$—5 gm., NaI—75 gm., water —100 cc. In making tests use at least as much reagent as alkaloidal solution and mix the test drop well so that any AgI precipitated by the dilution will be dissolved.

(59) *Lead sodium iodide.* Lead acetate—3 gm., NaI—100 gm., water—60 cc. Use at least as much reagent as alkaloidal solution, in doubtful cases twice as much. Mix the test drop to dissolve PbI_2 precipitated by dilution. This is not a satisfactory reagent for sensitivity determinations because of the precipitation of PbI_2.

Despite their defects both the silver and lead iodide reagent are of great value for crystals.

(60) *Platinum iodide & NaI (in excess).* H_2PtCl_6 crystals—1 gm., NaI—25 gm., water—100 cc. This is a deep purple-red solution. With only enough NaI to form H_2PtI_6 the solution is not stable and gradually deposits a black precipitate. Also crystals seem more likely to form with an excess of NaI. The reagent is too deeply colored to have much value for sensitivity determinations.

(61) *Dragendorff's reagent.* (Bismuth potassium iodide, acid.) Bismuth subnitrate—5 gm., KI—25 gm., water—88 cc., H_2SO_4 (1 + 9)—12 cc. This formula is intended to contain no more potassium iodide and acid than are necessary to insure satisfactorily against precipitation of BiI_3 or BiOI in the test drop. With this formula the reagent will keep in fair condition for several months, but it will not last indefinitely, as the hydriodic acid decomposes, yielding iodine.

Double-strength Dragendorff reagent. Bismuth subnitrate—10 gm., KI—45 gm., water—90 cc., H_2SO_4 (1 + 3)—10 cc. This is used principally as a stock solution to prepare the strongly acid Dragendorff reagent (following).

(62) *Strongly acid Dragendorff reagent.* Dilute a portion of the double-strength Dragendorff reagent with an approximately equal volume of (1 + 3) H_2SO_4. This reagent will not keep long. It is used to obtain maximum sensitivity to very weak simple bases.

(63) *Double-iodide Dragendorff reagent.* Bismuth subnitrate—5 gm., KI—50 gm., water—88 cc., H_2SO_4 (1 + 9)—12 cc.

Also, for a form of the reagent both strongly acid and containing a large excess of potassium iodide, take of the double-iodide reagent 5 cc., of 1:2 KI solution 6 cc., of (1 + 3) H_2SO_4 2½ cc.; mix. For strong alkaloids dilute H_2SO_4 instead of (1 + 3) H_2SO_4 could be used.

(64) *Antimony potassium iodide, acid.* The reagent will not keep more than a few days, so it is best to make it up when wanted

from a tartar emetic stock solution. Keep a solution of 5 gm. tartar emetic in 100 cc. water. As a reagent for strong alkaloids, take 6 cc. of the tartar emetic solution, add 2 cc. water, 6½ gm. KI, and 2 cc. (1 + 3) H_2SO_4. As a reagent for very weak alkaloids take 6 cc. of the tartar emetic solution, add 6½ gm. KI and 4 cc. of (1 + 3) H_2SO_4; no additional water. The antimony potassium iodide reagent gives results closely similar to those with Dragendorff's or the double-iodide Dragendorff reagent.

(65) *Stannous sodium iodide, acid.* Treat 3 gm. tin with 25 cc. concentrated HCl. When evolution of hydrogen has apparently ceased add 75 cc. water and ½ gm. excess tin. Keep this as a stock solution; the reagent itself will not keep long. For use add to 4 cc. of the $SnCl_2$ solution 2 gm. NaI. The solution is yellow; solid SnI_2 is orange, and a little of it may separate out as needles in the test drop, as a result of dilution. The reagent is very valuable for crystals.

(66) *Potassium iodide.* A 5 per cent. solution of KI. This has a very limited use, as it is not sensitive. With insoluble very weak alkaloids, such as pseudomorphine, it may act as a basic reagent. When it is necessary to guard against this, add a little acetic acid. (This applies also to all the other neutral iodide reagents.) In other cases, as in testing dibasic alkaloids such as quinidine, it may be necessary to guard against excessive acidity by adding a little sodium acetate.

VIII. Cyanides.

(67) *Potassium ferrocyanide.* A 5 per cent. solution of $K_4Fe(CN)_6$. This reagent will not keep indefinitely. Fresh, it is nearly colorless, but it gradually turns yellow.

(68) *Potassium ferricyanide.* A 5 per cent. solution of $K_3Fe(CN)_6$.

(69) *Sodium nitroprusside.* (Sodium nitroferricyanide.) 25 gm. in 100 cc. water. A 5 per cent. solution can be used but it will not keep. It gradually turns blue. The concentrated solution will keep indefinitely.

The above three reagents, and particularly the ferrocyanide, may act as basic reagents in precipitating very weak insoluble alkaloids. When it is necessary to guard against this, acidify the reagent with acetic acid or mineral acid.

(70) *Platinum cyanide reagent.* Dissolve 5 gm. H_2PtCl_6 crystals and 7½ gm. NaCN in 90 cc. water and heat the solution (which has an alkaline reaction) on the water bath. It soon begins to darken and assumes a red-brown color. Then remove and cool. Filter if there is any brown precipitate. (This forms if the heating is too prolonged, and a little is likely to be present.) Acidify the filtrate by adding 10 cc. of (1 + 3) H_2SO_4. *Caution!* HCN is given off! The acidified solution is the reagent. It is brown, but not much deeper in color than the 5 per cent. platinic chloride solution. It gives white precipitates with alkaloids.

(71) *Gold cyanide reagent.* Dissolve 5 gm. $HAuCl_4$ crystals in 100 cc. water and add NaCN little by little until the yellow precipitate that is formed dissolves to a colorless solution. This requires about 2½ gm. NaCN. The resultant solution must not turn red litmus blue. Should it do so, because of the addition of a little too much NaCN, acidify with acetic acid. This reagent gives white precipitates with alkaloids.

IX. Thiocyanates.

(72) *Platinum sodium thiocyanate.* H_2PtCl_6 crystals—5 gm., NaSCN—1½ gm., water—100 cc. Warm the solution on the water bath until it becomes red-orange. This formula does not contain enough NaSCN for the complete conversion of the platinum compound to thiocyanate, but in some tests seemed to be slightly more sensitive than a form with more NaSCN. However, the sensitivity varies but little with the NaSCN, and 4½ gm. can be used if desired, corresponding to $H_2Pt(SCN)_6$, and giving practically the same reagent. It is not advisable to use KSCN to make the reagent, as $K_2Pt(SCN)_6$ is not very soluble.

(73) *Mercuric potassium thiocyanate.* Dissolve 3 gm. KSCN in 100 cc. water and saturate with $Hg(SCN)_2$. (About 5 or 6 gm. required.)

Or (a) treat a 5 per cent. $Hg(NO_3)_2$ solution with KSCN until the precipitate of $Hg(SCN)_2$ just dissolves.

Or (b) $HgCl_2$—5 gm., KSCN—5 gm., water—100 cc.

The precipitating agent is $K_2Hg(SCN)_4$.

(74) *Zinc sodium thiocyanate.* Zinc acetate—5 gm., NaSCN—10 gm., water—100 cc. Forms $Na_2Zn(SCN)_4$.

(75) *Cadmium sodium thiocyanate.* $CdCl_2$—5 gm., NaSCN—18 gm., water—100 cc.

(76) *Cobalt sodium thiocyanate.* $Co(NO_3)_2$—5 gm., NaSCN—6 gm., water—100 cc. The reagent has a pink-red color but gives blue precipitates with alkaloids. The precipitating agent would seem to be $Na_2Co(SCN)_4$.

(77) *Ferric sodium thiocyanate.* $Fe_2(SO_4)_3$—1 gm., NaSCN—5 gm., water—100 cc. Only 1 gm. of $Fe_2(SO_4)_3$ is used in order to reduce somewhat the depth of color of the reagent. Even so, it is a very deep red.

(78) *Stannous sodium thiocyanate, acid.* The reagent, being decidedly acid, will not keep. As a stock solution treat 3 gm. tin with 25 cc. concentrated HCl, and when evolution of hydrogen has ceased add 75 cc. water and ½ gm. tin. (Same as for stannous sodium iodide, acid.) To 10 cc. of this solution add 1½ gm. NaSCN for the reagent.

(79) *Nickel sodium thiocyanate.* Nickel acetate—5 gm., NaSCN—6½ gm., water—100 cc.

(80) *Manganous sodium thiocyanate.* $MnSO_4.2H_2O$—5 gm., NaSCN—15 gm., water—100 cc.

(81) *Ammonium thiocyanate.* A 5 per cent. solution of NH_4SCN.

X. Nitrites.

(82) *Mercuric sodium nitrite.* $Hg(NO_3)_2$—5 gm., $NaNO_2$—4 gm., water—100 cc. Add a few drops of HNO_3 to make a clear solution. The formula corresponds to $Na_2Hg(NO_2)_4$. Sensitivity requires 3 to 7 gm. $NaNO_2$. This reagent seems to keep pretty well.

(83) *Mercuric sodium chloro-nitrite.* $HgCl_2$—5 gm., $NaNO_2$—5 gm., water—100 cc. This is somewhat more sensitive than mercuric sodium nitrite made with $Hg(NO_3)_2$. The presence of chloride is objectionable unless it is clearly realized that this is not a pure nitrite reagent.

(84) *Sodium cobalti-nitrite.* A 5 per cent. solution of $Na_3Co(NO_2)_6$. The solution has a brown color. It is not a very stable reagent. When the color of the solution has changed to pink, the nitrite has disappeared. The usefulness of the reagent can be restored (at least partially) by adding $NaNO_2$.

(85) *Lead copper sodium nitrite.* Lead acetate—6 gm., copper acetate—3½ gm., $NaNO_2$—10 gm., water—100 cc. This is a dark green solution. The compound is said to be $Na_2PbCu(NO_2)_6$.

(86) *Lead sodium nitrite.* Lead acetate—5 gm., $NaNO_2$—5 gm., water—100 cc.

XI. Organic Reagents.

(87) *Picric acid.* A saturated aqueous solution.

(88) *Tannic acid.* A 5 per cent. aqueous solution.

(89) *Tannic acid and sodium acetate.* Tannic acid—5 gm., sodium acetate—10 gm., water—100 cc.

(90) *Saccharin* (*sodium saccharate*). Take 5 gm. saccharin, add 70 cc. water; add 10 per cent. NaOH a little at a time until the saccharin is dissolved; make up to 100 cc. with water. The reagent should be acid to litmus. It may be advantageous to include ½ gm. benzoic acid with the saccharin, as a preservative.

(91) *Alizarin sodium sulphonate.* A 1 per cent. solution.

TWENTY YEARS OF "CO-FE-CU" FLUIDS

By H. V. Arny, Ph. D.

IF THE definition "Science is classified knowledge" is correct, this is not a scientific paper. Although it describes research work of the past twenty years, it can scarcely be considered as historical. As merely personal reminiscences it would not justify the writing and the printing. It is, in truth, a combination of the scientific and the historical represented by twenty years of work, that has been frequently interrupted by demands on the time of a busy teacher. It is written with the sole purpose of giving experiences that may be of value to the cause of pharmaceutical research. Since the paper is largely reminiscent I will drop the editorial "we" and will employ the first person singular.

"Co-Fe-Cu" fluids came into being through experimentation undertaken in behalf of the Revision Committee of the National Formulary. In 1910 a special sub-committee was chosen by that committee to study the question of the standardization of the color of certain N. F. preparations. The first two years of work of this sub-committee was devoted to the study of the then known methods of color standardization with the result that none of these were found adaptable for N. F. purposes. In searching for a new device, I first asked myself whether there were a group of inorganic salts, red, yellow and blue, which could be made into solutions and blended to form colors other than the three primary tints. These salts I found in cobalt chloride, ferric chloride and copper sulphate. After a crude testing of the feasibility of the method I prepared from these salts half normal solutions and from these half-normal solutions a set of ninety-one different blends. These I exhibited at the Eighth International Congress of Applied Chemistry held in New York City in September, 1912, reading before the Section on Pharmaceutical Chemistry of that Congress my first paper on these "Co-Fe-Cu" fluids (a).

Diligent search in 1912 of previous literature failed to show that this idea of mine had ever been published before. I did find that Allen Hazen (b) had devised a test for the color of potable water based on mixing empiric solutions of platinic chloride and cobalt chloride, but this fact was not discovered by me until the three "Co-Fe-Cu" colored fluids and their blends had been definitely for-

mulated and prepared. At this time it might be well to state the following interesting points that have developed during the preparation and study of "Co-Fe-Cu" fluids and their blends.

1. The devising of standard colored fluids of definite strength and color intensity that can be standardized by simple volumetric methods, that can therefore be easily duplicated and that twenty years of observation have proven to be permanent.

2. The discovery that these half-normal solutions when prepared without the addition of acid had equal color value; that equal volumes of these fluids upon admixture gave a "neutral gray" fluid. In short, that equimolecular solutions of the cobalt, iron and copper salts were equal in color.

3. As the unacidulated solutions, when blended, precipitated after standing a few months, subsequent solutions were made with 1 per cent. hydrochloric acid. The acidulated solutions constitute the "Co-Fe-Cu" fluids and are more stable than the glass containers in which they are stored.

4. The color values of the "Co-Fe-Cu" fluids were carefully checked against the glasses of the Lovibond tintometer. Their spectrophotometric readings were made and published by Mellon and Martin (c). They have been used for preparing matches of:

1. Nessler ammonia colorimetric test (d).
2. Nitrate colorimetric water test (d).
3. Cottonseed oil (e).
4. Liquid petrolatum color test (f).
5. Suprarenal colorimetric assay (f).
6. pH matching standards (g).

5. The preparation of these standardized colored fluids were reduced to pharmacopœial style in the following description published in 1923 (f).

Colorimetric Cobalt T. S.—Dissolve 59.4965 grams (or 59.5 grams) of cobalt chloride, $CoCl_2.6H_2O$, in enough of a fluid made by mixing 25 cc. of hydrochloric acid U. S. P. with 975 cc. of distilled water to make 1000 cc. of test solution. This test solution should be standardized to the above half-normal strength by the following assay: Place 5 cc. in a 250 cc. flask; add 15 cc. of 20 per cent. sodium hydroxide and 5 cc. of solution of hydrogen dioxide (3 per cent.), boil for ten minutes, cool, add 2 grams potassium iodide, followed by 20 cc. sulphuric acid (1:4). When the precipitate has dissolved titrate with tenth-normal sodium thiosulphate. Each cubic centimeter of $N/10$ thiosulphate corresponds to 0.023799 gram $CoCl_2.6H_2O$.

Colorimetric Ferric Test Solution.—Dissolve about 50 grams of ferric chloride U. S. P. in enough of a fluid made by mixing 25 cc. of hydrochloric acid U. S. P. with 975 cc. of distilled water, to make 1000 cc. of test solution. This test solution must be standardized to half-normal strength (45.054 grams $FeCl_3.6H_2O$ to the liter) by the hydrochloric acid, potassium iodide, sodium thiosulphate volumetric assay, found under *Ferri Chloridum;* 10 cc. of the test solution being employed. Each cubic centimeter of $N/10$ thiosulphate corresponds to 0.027032 gram $FeCl_3.6H_2O$.

Colorimetric Copper Test Solution.—Dissolve 62.43 grams of copper sulphate, $CuSO_4.5H_2O$, in enough of a fluid made by mixing 25 cc. of hydrochloric acid U. S. P. and 975 cc. of distilled water, to make 1000 cc. of test solution. This test solution should be standardized to the above half-normal strength by the acetic acid, potassium iodide, sodium thiosulphate volumetric assay, found under *Cupri Sulphas;* 10 cc. of the test solution being employed. Each cubic centimeter of $N/10$ thiosulphate corresponds to 0.024972 gram $CuSo_4.5H_2O$.

So much as to basic information concerning the "Co-Fe-Cu" fluids. Let us now turn to the recognition accorded these fluids by impartial observers.

1. One of the earlier papers, mildly objected to in 1914 by the editor of the *Journal of Industrial and Engineering Chemistry* because of its length, was republished from that journal in full and in serial form by the *Chemical News* of London (h).

2. Mellon and Martin, in the *Journal of Physical Chemistry,* published spectrophotometric readings of the "Co-Fe-Cu" blends (c).

3. Recently Mehlig and Mellon, in the *Journal of Physical Chemistry,* described at length the Taub application of the "Co-Fe-Cu" blends in the preparation of stable pH standards (e).

4. In the Tschirch "Festschrift" the only paper of American origin was a description of these colored fluids. It is moreover the only paper in the book printed in English (g).

5. The American Pharmaceutical Association in 1924 accorded the Ebert Medal to H. V. Arny and A. Taub for their work on the "Co-Fe-Cu" colored fluids.

Why then do we hear so little of these colored fluids? The answer to this query can be reduced to three words: lack of propaganda.

When I realized the importance of these fluids, I thought of patenting the idea and placing it upon a commercial basis. Had I done so the fluids would have been in general use today. But, back in 1912-1914, I had the old-fashioned notion of scientific ethics: that the results of pure research belonged to the entire scientific world

rather than to the individual. I did approach a then existing research group which was accepting ideas offered by inventors, patenting same and devoting the financial returns from same to educational purposes. From this group, however, I received only a polite letter of declination. I then attempted to popularize the idea on a large scale by choosing the color of cottonseed oil as a subject of research. All of this oil is sold on the wholesale scale upon its color value and back in 1913-1918 the color standards set for the various types of oil (blends of Lovibond glasses) were subject to severe criticisms (k). The committee of the oil chemists expressed great interest in the "Co-Fe-Cu" colors and invited me to their annual meeting in New Orleans but circumstances hindered my going. The meeting was attended by the representative of an optical concern and upon his persuasion there was tentatively adopted an apparatus costing over $200 that proved its uselessness after two years of experimentation. The only outcome of my expedition into the field of cottonseed oil was a request made to me to furnish my standard color fluids to an oil concern in ten-gallon lots and apparently the price I set was too steep, since I heard nothing further from the firm.

We now reach the interesting question as to the value or lack of value of the "Co-Fe-Cu" colors. Their advantages may be summarized as follows:

1. They are scientific, since based on molecular proportions.
2. They are practical, since based upon normality figures, making them as easy to prepare as volumetric solution.
3. They are inexpensive.
4. From them innumerable color blends may be prepared.
5. They are more stable than the glass containers in which they are stored. The fluids made in 1912 to 1914 still hold their original Lovibond readings, but the glass containers used have become distinctly foggy, even as old glass bottles have a way of doing.

With all these advantages to their credit, why have these fluids failed to receive general acceptance? Before venturing an answer to this question, I will say that I have never noted a single criticism of this method of measurement of transparent colors. No claim has ever been made by me as to their basic superiority from the stand-

point of purely physical measurement. The modern type of spectrophotometer giving as it does color readings in terms of spectral wave length is of course the true basis of color measurement. There is no idea of replacing this basic apparatus with the "Co-Fe-Cu" fluids where exact measurement is required. The spectrophotometer is, however, a very expensive instrument, far beyond the financial reach of the average laboratory, and its manipulation requires skill that comes only from experience. For routine color matching, the "Co-Fe-Cu" colors have the advantages of simplicity, speed and cheapness.

What disadvantages do these fluids possess? So few are the disadvantages that the query had better be converted into the words, "Why have the 'Co-Fe-Cu' fluids lacked popular appeal?" Here are the reasons that suggest themselves to me:

1. The modern chemist, like all other moderns, is looking to machines as aids, rather than to cheaper methods involving hand work. So simple a task as preparing a volumetric solution is rejected if a mechanical device is offered as a substitute. Do we not in truth have chemical supply concerns who now furnish the "busy chemist" with volumetrics in concentrated form?

2. Advertising propaganda affects all of us. A method offered free to the chemical world is less apt to be successful these days than a device affording sufficient profit to the exploiter to justify extensive advertising.

3. While the preparation of each of the three basic colorimetric fluids is a relatively simple task, the preparing of color matches is exceedingly difficult, because of the enormous number of hues that can be prepared from the three basic fluids. In preparing matches for the commercial color types of cottonseed oil, over 100 color blends were prepared and matched. Thus the color of "prime white" oil ranged roughly between these two dilutions; (a) 13.2 cc. of n/2 ferric chloride, 1.1 cc. of n/2 cobalt chloride and water to make 50 cc., and (b) 15.5 cc. of the ferric solution, 0.8 cc. of the cobalt solution and water to make 50 cc.; yet no less than twenty blends between these two were prepared in order to reach successful and practical matches.

The match once secured and reported, it affords a simple and stable color standard that can be readily duplicated by any chemist of average ability. However, the pioneer work of setting the standard is a matter of patient and painstaking effort, which illy fits in with the hectic *tempo* of today.

It is not in the spirit of petulance that I express a deep regret over the fact that during the past twenty years I have not had adequate aid in my work on these "Co-Fe-Cu" colored fluids. The work performed by my co-workers, Messrs. Ring and Taub, each devoting about one year to the work, convinces me that with five research assistants a year for the twenty years, color standards for practically all of the colorimetric tests and for the leading pharmaceuticals would now be in practical use. This brings me to the last thoughts, not so much in connection with the "Co-Fe-Cu" fluids, but with pharmaceutical research in general, these thoughts can be reduced to five propositions:

1. Much of the research confronting pharmacy of today involves months of labor.
2. The modern research man in pharmacy, be he teacher or scientist in manufacturing plant, after he has obtained reputation and maturity, is so busy with the details of his everyday life, be these details of administration or of mere subsistence, that he has little or no opportunity for personal research.
3. If the research ability of this type of pharmacist is to be utilized to advantage it is imperative that he shall have at his disposal one or more well-trained young men whose entire time is devoted to research under the personal direction of their superior officer.
4. For this reason all forward-looking colleges of pharmacy should have graduate courses (beyond B. S. degree) wherein a large percentage of the time is devoted to research.
5. Such graduate courses should be aided by the creation of research fellowships providing enough income to finance the Fellow during his graduate years.

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February, 1932.

THE INTRODUCTION OF LOBELIA SYPHILITICA INTO MEDICINE

By Rodney H. True

SOME years ago while looking up the story of the old preacher-physician, Jared Eliot, of Killingworth (now Clinton), Connecticut, I encountered his medically more eminent son-in-law, Dr. Benjamin Gale, perhaps his favorite pupil. Dr. Gale had a widespread reputation in the northern colonies, as is made clear by a correspondance that I had the good fortune to unearth some years ago in the Library of Congress at Washington.

It is generally known that the use of *Lobelia syphilitica L.* against venereal disease is traced back to the New York Indians as appears in a communication from the Swedish botanist and traveler, Peter Kalm. Since certain details can be traced in the correspondence above alluded to, it seems to be worth while perhaps to bring it to light.

It opens with a letter from Dr. Benjamin Gale, dated October 26, 1767, at Killingworth, addressed to Rev. Samuel Johnson, of Stratford, Connecticut, who was supposed to have access to Sir William Johnson, member of the Governor's Council of the New York Colony, who was supposed to have full information on the subject of interest.

Dr. Gale writes: "Reverend and Dear Sir: Reading the other day Dr. Haller's Medical Cases and Experiments, communicated to the Royal Academy of Sciences at Stockholm, among other things I find a remedy for the Venereal Disease discovered by Peter Kalm, being a plant used by the Natives of America for the cure of that Disease, which by the Influence of Sir Wm. Johnson he obtained from the Savages which he terms *Lobelia.* This plant Dr. Haller says safely and expediciously cures the Venereal Disease, and more so than any mercurial preparation made use of by Europeans for the Cure of that Disorder. If this account be true, as it seems attested by so good a Voucher, I am of the Opinion it may be rendered of great service in the very worst diseases which affect the Human body, and which indeed are a reproach to the Medical Art, such as these, the Leprosy of the Greeks, Elephantiasis, the Canker which carries off Thousands of Youth, and old obstinate scorbutic cases. As I have a Patient who I greatly value laboring under the Leprosy, Joyned with a Scorbutic Habit, I should ever acknowledge the Favour, if you

would be so kind as to use your Friendship with Sr. William to gain the knowledge of this Plant, to procure some of it, as also some of the Seeds, and ye knowledge of the place or Soils best adapted to its Growth. . . . The method in which the natives use it, would likewise be necessary to know, and its Operation, if it operates any other ways than an Alterative. . . .

"If I may be favourd with such informations, I shall, with his permission, endeavor in the most extensive manner, to render them of publick Utility, and if I may be permitted, Acquaint the Publick, to whose Benevolence and Goodness they are indebted for the Discovery, which I am under some advantage to communicate, either by the Royal Society or the Colledge of Phisitians at Edinburgh."

To this appeal Rev. Samuel Johnson seems to have listened sympathetically since in the Library of Congress there appears a letter from him to Sir William Johnson dated at Stratford, Connecticut, November 2, 1767. He qualifies Dr. Gale as an expert and leaves his plea with Sir William.

"This Dr. Gale is I believe the most considerable physician in these parts. He had an Academical Education, and was regularly bred to physick by the celebrated Dr. Elliot, of whom, perhaps you may have heard. He is very ingenious and inquisitive, & has a correspondence with the famous Dr. Huxham in England and other members of the Royal Society, & being a friend of mine, I humbly hope you will excuse my thus writing to you at his desire."

Sir William's reply, to be seen in the Library of Congress, was promptly penned. He writes from his historic mansion still to be seen by the interested tourist. "Johnson Hall, December 23rd, 1767. Since my last of the 1st of this Inst., I was favoured with yours of the 2nd November inclosing (Doctor Gale's) letter to whose Ingenuity, Abilities and Character I could not refuse the Satisfaction he recognizes concerning the plant which Dr. Haller considers as Efficacious in The Cure of the Venereal Disorder touch(ing) which I must acknowledge the Truth of Dr. Gale's information. . . . Mr. Kalm an Ingenious Botanist from Sweden, on a tour through this Country for obtaining Usefull Subjects in the Way of his Study in the year (blank space) applied to me for advice & Countenance to Enable him to prosecute his design, which he readily obtained with a Protection & Escorts of Indians that enabled him to go as far as the Great Falls of Niagara, then deemed a bold Undertaking. In a

Conversation with this Gentleman on his return concerning the many Medicinal plants, which are used with Great Success by the Indians, I took occasion to mention that which is the Subject of this Letter and Gratified his enquiries about it with an Exact Description of the plant & an acct. of its Extraordinary Effects—by which means it came to the Knowledge of Dr. Haller, but how far that Eminent Physician has been enabled to describe it I can't tell. I shall therefore readily give Dr. Gale all the Information I can as well as procure him the plant when the season permits, heartily wishing it may thro' his Means be introduced and be found beneficial to the publick in Cases he Describes.

"This plant as near as I can at present recollect has many white Fibrous Roots & grows in the stalk to be about 2 feet in heighth bearing a flower the Cup of which is in the form of a bell, and of a fine Blue Colour. It grows only in cold Swampy Grounds, and is to be found in many parts of this Country particularly on one part of my estate, from whence I furnished Mr. Kalm with the Specimen. The Indians use it both as a Decoction and Lotion. They boil the Roots, the Juice of which they Drink washing the parts Likewise with the Liquid. They also use it with great success in Disorders of the Bowells, but the former I shall fully Describe in the Manner required and also procure them for Dr. Gale as soon as possible in the Spring, for at present we have Two feet of snow hereabouts so that it cannot be had—and this must at present apologize, for the imperfect description I have given of it . . ."

The correspondence seen closes with a brief note dated at Stratford, March 21, 1768, in which Rev. Samuel Johnson gratefully acknowledges the foregoing communication that Dr. Gale was likewise "vastly obliged" to receive.

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QUALITATIVE TESTS FOR THE DETECTION OF ROSIN, ROSIN OIL AND HEAVY METALS IN LINSEED OIL

By James J. Deeney

BOILED oil, which is used in the paint, printing ink, and allied industries, contains small amounts of metallic driers—usually lead and manganese. This oil is somewhat darker in color and more viscous than raw linseed oil and generally gives a positive reaction for rosin, as well as heavy metals, as the driers are often incorporated in the form of resinates.

The U. S. P. should include under the caption of "Tests for Purity" sufficient directions for distinguishing a medicinal oil from one intended for technical purposes. The presence of heavy metals, rosin or rosin oil indicates a technical purpose oil unfit for medicinal use.

The U. S. P. X does describe a method for detecting rosin or rosin oil in linseed oil: "Two cc.'s of oil and an equal volume of glacial acetic acid are warmed in a test tube, allowed to cool, and one drop of sulphuric acid is added. A violet coloration denotes the presence of rosin or rosin oil."

The observation of this color reaction in a test tube, the selection of glacial acetic acid as a solvent for rosin or rosin oil, and the use of concentrated sulphuric acid makes the U. S. P. X test, which is supposed to be a modification of the "Lieberman-Storch reaction" practically worthless.

Color reactions, even under the most favorable conditions are not wholly reliable. The fugitive violet reaction indicative of rosin dissipates rapidly and cannot be observed satisfactorily in a test tube. A white porcelain spot plate should be used. Solutions containing 1 per cent., 5 per cent. and 10 per cent. of rosin and rosin oil respectively, all failed to give the characteristic violet coloration when observed in a test tube.

The original and other modifications of the "Lieberman-Storch reaction" specify acetic anhydride, while the U. S. P. X directs the use of glacial acetic acid. The purpose of the acetic anhydride is to act as an immiscible solvent and separate the rosin or rosin oil from the linseed oil. When heated to 65 degrees C. linseed oil and acetic anhydride are miscible; below this temperature the oil and anhydride

are immiscible, and the rosin oil or rosin, if present, is transferred to the acetic anhydride layer. At room temperature glacial acetic acid and linseed oil are almost completely miscible, therefore, this acid does not play the part of an immiscible solvent but acts only as a diluent.

Concentrated sulphuric acid carbonizes organic substances. As numerous tests conducted with concentrated acid gave a reddish to dirty brown coloration when one drop of acid was added, even on a spot plate, to acetic anhydride extracts of linseed oil containing small amounts of rosin, it was concluded that the strength of the acid was such that it interfered with the sensitiveness of the test, masking the fugitive violet coloration. A mixture of equal parts of sulphuric acid and water gave excellent results, a clean-cut violet reaction resulting with oils containing as low as one-half of 1 per cent. of rosin.

The following method for the detection of rosin and rosin oil which is not original but the procedure usually employed in the paint and oil industries was found to give a positive Lieberman-Storch reaction in the presence of minute amounts of rosin or rosin oil: Three cc.'s of linseed oil are warmed gently in a test tube with an equal quantity of acetic anhydride. The mixture is allowed to stand until a clear separation takes place. The lower anhydride layer is pipetted off and transferred to the several depressions of a white porcelain spot plate. One drop of dilute sulphuric acid (mix equal parts of sulphuric acid and water and cool to room temperature) is added by means of a glass stirring rod to one of the depressions containing the anhydride extract, and the coloration produced noted. A brown or greenish coloration is ignored, but a fugitive violet coloration denotes the presence of rosin or rosin oil.

The U. S. P. X does not include a test for "heavy metals" under linseed oil. This is unfortunate as linseed oil intended for technical purposes which may contain lead and manganese as linoleates may possibly find its way into the drug trade. At least precaution should be taken to guard against such a possible error. The following method may be used to detect the presence of heavy metals in linseed oil: Three cc.'s of linseed oil are ignited and incinerated to ash in a small porcelain crucible. The ash is dissolved with a few drops of a mixture of nitric and hydrochloric acid and evaporated gently to dryness. The residue is then leached out of the crucible with a small portion of distilled water and the solution filtered. The filtrate is neutralized with ammonia water, made slightly acid with hydrochloric acid and tested for heavy metals as directed by the U. S. P. X.

SMOKE—FLASH—FIRE POINTS OF CERTAIN FIXED OILS

By Wallace H. Dickhart

KNOWING that there is existent very little data in tabulated form in regard to the smoke, flash and fire points of various commercial oils, it is thought that a list such as follows will be of use to those interested.

These results were obtained by employing the Cleveland Open Cup method and are not the average of a number of samples of the same oil. The tests were made at different intervals and therefore are but approximate values. Nevertheless, they give fairly accurate limits and indicate at what degrees temperature the oils should smoke, flash and fire.

Oils	Smoke F°	Flash F°	Fire F°
Olive (edible)	350 "	554 "	690 "
" (commercial)	290 "	538 "	682 "
" (bleached refined foots containing CS_2)	348 "	570 "	670 "
Rapeseed	256 "	680 "	692 "
"	412 "	600 "	692 "
"	332 "	594 "	692 "
" (English)	390 "	614 "	692 "
Sesame	500 "	632 "	684 "
Palm (Refined)	446 "	620 "	692 "
Cottonseed (P. S. Y.)	493 "	616 "	680 "
" (Deodorized)	508 "	650 "	680 "
Peanut	464 "	632 "	692 "
Hydrogenated Cottonseed	380 "	590 "	660 "
Soya Bean	280 "	580 "	... "
Lard Oil	288 "	492 "	610 "
Tallow (Acidless)	... "	605 "	695 "
" (2% F. F. A.)	350 "	545 "	675 "
Red Oil	260 "	368 "	414 "
Sperm	130 "	510 "	672 "
Pine	... "	153 "	184 "
Turpentine	... "	84 "	98 "

MEDICAL AND PHARMACEUTICAL NOTES

THE RELATIVE ACTIVITY OF ERGOTOXINE AND ERGOTAMINE—Quite considerable opinion exists regarding the relative physiological activity of ergotoxine and ergotamine. The data presented by the authors have been obtained, not with any definite object of differentiating between the activities of the two alkaloids, but as a result of experimental work on the preparation and biological evaluation of a tartaric acid salt of ergotoxine.

They start out by stating that ergotoxine and ergotamine do not appear to possess equivalent biological activity and the relative color reaction of the two alkaloids is not parallel with their relative biological activity.

After a brief historical account of the work of other investigators they present their experimental work with quite some detail. All the biological and colorimetric determinations were made with fresh solutions.

They arrive at the following conclusions:

1. Ergotoxine is about 66 per cent. more active than ergotamine when compared by the biological method of Brown and Clark. This is qualitatively the same result as that obtained by Pattee and Nelson, who reported a 33 per cent. greater activity of ergotoxine in an impure compound.

2. Pure ergotoxine or its salts would appear to be a more suitable standard of reference for the biological assay of preparations made from ergot of rye.

3. The color reaction of ergotamine is distinctly greater than that of ergotoxine and hence is not parallel with the biological activity relation of the two alkaloids.

Summary

1. An alkaloidal tartrate, corresponding to ergotoxine di-tartrate, has been prepared from Spanish ergot.

2. The biological activity and color reaction of this compound in relation to ergotoxine ethanesulphonate, ergotamine methanesulphonate and ergotamine tartrate have been studied.

3. It has been shown that ergotoxine is biologically more active than ergotamine and the quantitative relation has been indicated.

4. It has been shown that ergotamine is more active colorimetrically and less active biologically than ergotoxine. By E. Lozinski, G. W. Holden and G. R. Driver, *Journal of Pharmacology and Experimental Therapeutics,* No. 2, June, 1931.

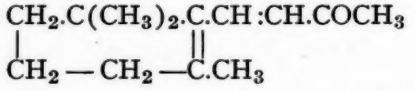
J. K. T.

VITAMIN A AND IONONE—Vitamin A, the food substance necessary to produce normal growth, has just been shown to be closely related to a well-known perfume, artificial violet, by Prof. Paul Karrer, of the Chemical Institute of the University of Zurich, who has proposed a chemical formula for the vitamin.

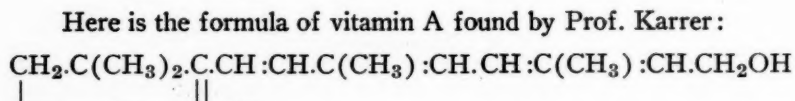
Ionone, the basic material of all violet perfumes, and one of the most important synthetic products in the art of perfumery, forms the larger part of the molecule of vitamin A in Prof. Karrer's formula. Only beta ionone, however, one of two closely related forms of ionone, is present in the vitamin.

Vitamin A is the vitamin that has recently been obtained by Prof. J. C. Drummond and his associates of University College, London, by breaking in two the substance carotin, the well-known yellow pigment of carrots, butter and egg yolk.

The chemist's formula for the violet perfume, beta ionone, looks like this:



Here is the formula of vitamin A found by Prof. Karrer:



which, one can see, contains the ionone grouping without alteration.

The six carbon ring on the left of both formulas is commonly found in the class of "terpene" substances, of which turpentine and camphor are familiar examples. The remainder of the vitamin formula is partly related to the isoprene unit of the rubber molecule and is an alcohol similar chemically to ethyl or grain alcohol.

The new formula was proposed in the Swiss chemical journal, *Helvetica Chimica Acta.*—(*Science Service.*)

X-Rays Detect Lead Poisoning in Children—A new method of diagnosing lead poisoning by means of X-rays has been reported to the American Medical Association by Dr. Edward C. Vogt, of the Infant's Hospital and the Children's Hospital in Boston. When lead is absorbed into the body it is stored in the bones and can be detected in the X-ray pictures as a dense band at the growing margin. Its elimination following treatment can also be observed by means of X-ray pictures.

The author pointed out that lead poisoning is a frequent and serious condition in children and one not always easy to diagnose. The dark line, called the lead line, at the margins of the gums is significant of the disease in adults but is seldom seen in small children, and the other diagnostic tests require considerable technical skill.

The most frequent source of lead affecting the health of infants and children is from paint off the furniture, woodwork and toys, and, as everyone knows, infants have a common tendency during the teething period to chew at anything they can get into their mouths.

When sufficient lead paint has been eaten in this way, symptoms of lead poisoning develop. This happens most often between the ages of one and two years.

The X-ray test for lead poisoning cannot be used alone, Dr. Vogt pointed out, as some other conditions give the same or nearly the same picture, but together with other evidence, such as a history of chewing painted toys, it is very useful.—(*Science Service.*)

Denicotinizing Tobacco With Silica Gel—Nicotine, together with harmful tarry stuffs and coloring matter, is taken out of tobacco smoke by tubes of silica gel inserted in pipe stems and cigarette or cigar holders, states a German chemical publication, *Zeitschrift*

für angewandte Chemie. The "smoke-sweetening" properties of silica gel were discovered by Prof. J. Traube. Silica gel is a common chemical, widely used as an adhesive and as an egg preservative. Smoke from bad cigars and cigarettes loses its "scratchy" quality when drawn through the gel, the report states. Even the rank tobacco grown in the German Palatinate is said to be rendered smokable by it.—(*Science Service.*)

Filterable Germs Outnumber Visible Ones in Milk and Soil—The filterable forms of germs, which are so small that they cannot ordinarily be seen even with the most powerful microscopes, far outnumber their larger, microscopically visible relatives in such substances as milk and milk products, soil, hay infusions and decomposing manure, experiments by Prof. J. M. Sherman and C. E. Safford, of Cornell University, show.

The ordinary forms of germs may be found by the million or even billion in one gram, which is roughly one-thirtieth of an ounce, in certain types of decomposing and fermenting materials. But the Cornell investigators found not millions but trillions of the minute organisms to the gram in some samples of milk, they reported to the journal, *Science.*

Contamination of milk and water with germs is ordinarily determined by a method of counting the number of microscopically visible germs or bacteria present in a given sample. But such examinations take no account of the invisible organisms which may be present. This class of invisible, filter-passing organisms is becoming increasingly important, especially since it has been found that some ordinarily visible germs may have an invisible stage.

The new method combines a series of dilutions of the material to be examined with a longer period for growth in broth at a temperature of about 86 degrees Fahrenheit.—(*Science Service.*)

Silver Filter Purifies Water—A new type of filter, with interstices covered with silver, has been tested at the Pasteur Institute of Paris by Dr. Nicholas Metalnikov, and found to confer upon the filtered water the power to destroy living bacteria.

The filter is made by adding chloride of silver to the moulding clay and baking at a high temperature of 2200 degrees Fahrenheit.

According to its inventor, Georges Lakhovsky, the water which passes through the filter does not contain any silver and is perfectly harmless; yet it retains for several days the power to destroy resistant bacteria like the common bacillus coli and bacillus typhosus, which causes typhoid fever.

The bactericidal power of the water that has passed through the silvered filter is claimed to be entirely due to the ionization of the water, and it disappears if the water is boiled for a few minutes. During its passage through the filter the water becomes slightly alkaline.—(*Science Service.*)

Successful Treatment of Drug Addiction Reported—Details of a successful treatment of a case of sixteen-year-long drug addiction with a chemical that thins the jelly-like consistency of the brain have just been reported to the National Academy of Sciences here by Prof. Wilder D. Bancroft and his associates, Dr. Robert S. Gutsell and John E. Rutzler, of Cornell University.

The chemical is sodium rhodanate. The "cure" of the human drug addict is the final bit of evidence in support of Prof. Bancroft's theory that in morphine addiction the jelly-like consistency of the brain becomes thicker, more gelatinous, or, as the scientists say, the brain colloids are agglomerated. The use of the method on a human subject followed observations of its usefulness in animals addicted to the drug.

The patient was a man forty-nine years old, a trained nurse, who had been addicted to the use of morphine for sixteen years, during which time he had been treated four times. The various methods used had been insensible withdrawal, slow withdrawal, abrupt withdrawal and the Towns-Lambert treatment. After one course of treatment, the patient did not use the drug for four months, but after the other withdrawals, he started using it again in from two days to three or four weeks. In six days he was withdrawn from the drug completely by the Cornell method of treatment, and has not used it since, a period of three weeks.

During a previous course of treatment the patient had been considered a "mean customer," and had suffered periods of severe depression, severe gastro-intestinal upset, and all the other withdrawal symptoms. When withdrawal was accompanied by appropriate doses of sodium rhodanate, none of these effects was observed. The patient had periods of restlessness, nervousness and sleeplessness, but these were found to be due to the fear that he had many days of suffering ahead of him before the morphine would be entirely withdrawn. He was astonished when told at the end of the ninth day of the course of treatment that he had had no morphine for twenty-four hours.

"Since the patient has been withdrawn he claims to have had no desire whatever for morphine, and our observations of him support his contention," Prof. Bancroft stated.

The fact that the craving for morphine can be controlled by sodium rhodanate means that mental rehabilitation will almost surely follow the treatment, he concluded.—(*Science Service.*)

VITAMIN C DERIVED FROM POISON FOUND IN OPIUM—The parent substance of the life-essential, scurvy-preventing vitamin C is none other than the poison narcotine, investigations of Dr. Otto Rygh, his wife, Dr. Aagot Rygh, and Dr. Per Laland here have shown. Narcotine is one of the alkaloid poisons found in opium and is related to morphine, but in spite of its name does not have any narcotic effect. It is transformed into vitamin C during the ripening of fruits and vegetables.

The isolation of vitamin C and discovery of its parent substance came as a result of studies of the occurrence of the vitamin in various fruits and vegetables such as oranges, lemons, tomatoes, white cabbages and potatoes. The Norwegian scientists found that narcotine was present in the unripe fruits but gradually disappeared as the ripening proceeded and the ripe products contained the vitamin but no narcotine.

Guinea pigs were then fed on a diet containing narcotine and on a diet containing narcotine that had been exposed to ultra-violet light; both groups of guinea pigs died at the same time, but the group that had been fed on the solarized product showed no signs of scurvy while the other group was severely affected with it.

It was next found that methylnarcotine, derived from narcotine, could prevent or relieve scurvy. It was also found that narcotine was converted into an anti-scorbutic by submitting it to the action of germinating seeds.—(*Science Service.*)

MERODICEIN — Monohydroxy-mercuri-di-iodo-resorcin-sulphonphthalein is one of the series of organic mercurial compounds synthesized by Dunning and Farinholt. The disodium salt of the compound has been named Merodicein. The authors of this paper found it to possess marked antiseptic properties. As this drug has been used experimentally by a number of physicians in the form of mouth washes and lozenges for antisepsis of the oral cavity and throat a toxicological study of it was deemed imperative.

A study of its toxicity for plants, paramecia, larvae of frogs, fish, mice, rats, guinea pigs, cats, dogs, and rabbits is set forth with much elaboration.

Its effect on the gastrointestinal tract was very carefully studied. Next to the kidneys the gastrointestinal tract is most affected by the administration of mercurials. Especially is this true of inorganic mercurial compounds, which produce a specific enteritis through the action of inorganic or ionic mercury. It is generally known that organic compounds of mercury are much less drastic in this respect.

Its effect on the circulation was also carefully studied. It is well known that the mercury ion produces a depressant effect on the circulation, particularly on the heart muscle.

The absorption and excretion of this drug was likewise studied.

Bacteriological findings were obtained by work done chiefly on the Staphylococcus aureus and Bacillus typhosus.

As the most important therapeutic use of merodicein is in the field of antisepsis as a bactericidal or bacteriostatic agent, their investigation gives abundant information as to its usefulness for such purposes. They found that when applied directly to isolated living plant or animal tissues, merodicein is not a very powerful protoplasmic poison.

They found that very little of the drug is absorbed through the intestinal walls and diverted to the kidneys so that their function remains unimpaired and even after large doses only a laxative effect

is noted. The laxative action resembles that of a saline. In view of their findings they think it warrants an extensive clinical trial as an antiseptic for the mouth and throat—David I. Macht and Helen M. Cook, *Jour. of Pharmacology and Experimental Therapeutics,* page 571, vol. 48, 1931.

J. K. T.